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(54) Title: NEW COMPOUND			
(57) Abstract			
<p>This invention relates to new polypeptide compounds represented by general formula (I), wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are as defined in the description or a salt thereof which has antimicrobial activities (especially, antifungal activities), inhibitory activity on <math>\beta</math>-1,3-glucan synthase, to process for preparation thereof, to a pharmaceutical composition comprising the same, and to a method for prophylactic and/or therapeutic treatment of infectious diseases including <u>Pneumocystis carinii</u> infection (e.g. <u>Pneumocystis carinii</u> pneumonia) in a human being or an animal.</p>			
<p style="text-align: right;">(I)</p>			

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## DESCRIPTION

## NEW COMPOUND

## TECHNICAL FIELD

5           The present invention relates to new polypeptide compound and a salt thereof which are useful as a medicament.

## BACKGROUND ART

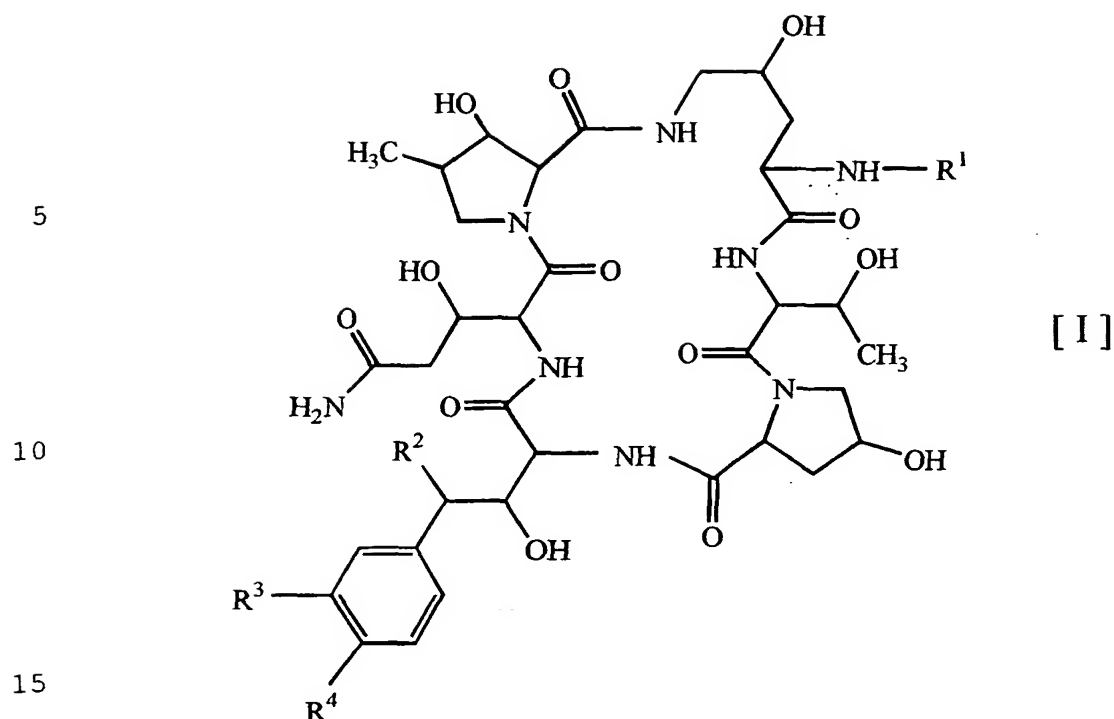
10           In U.S. Pat. No. 5,376,634 and WO 96/11210, there are disclosed the polypeptide compound and a pharmaceutically acceptable salt thereof, which have antimicrobial activities (especially antifungal activity).

## DISCLOSURE OF INVENTION

15           The present invention relates to new polypeptide compound and a salt thereof.

          More particularly, it relates to new polypeptide compound and a salt thereof, which have antimicrobial activities [especially, antifungal activities, in which the fungi may include Aspergillus, Cryptococcus, Candida, Mucor, Actinomyces, Histoplasma, Dermatophyte, Malassezia, Fusarium and the like.], inhibitory activity on  $\beta$ -1,3-glucan synthase, and further which are expected to be useful for the prophylactic and/or therapeutic treatment of Pneumocystis carinii infection (e.g. Pneumocystis carinii pneumonia) in a human being or an animal, to a process for preparation thereof, to a pharmaceutical composition comprising the same, and to a methods for the prophylactic and/or therapeutic treatment of infectious disease including Pneumocystis carinii infection (e.g. Pneumocystis carinii pneumonia) in a human being or an animal.

          The object polypeptide compounds of the present invention are new and can be represented by the following general formula  
35   [I]:



Wherein

- $R^1$  is      hydrogen;  
                   arylamino(lower)alkanoyl which may have one or more  
 20               suitable substituent(s);  
                   aroyl substituted with heterocyclic group which may  
                   have one or more suitable substituent(s);  
                   aroyl substituted with aryl having higher alkyl;  
                   aroyl substituted with aryl having lower alkyl;  
 25               aryl(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having  
                   lower alkyl;  
                   lower alkanoyl substituted with unsaturated  
                   condensed heterocyclic group which may have one or more  
                   suitable substituent(s);  
 30               lower alkanoyl substituted with pyridyl which may  
                   have one or more suitable substituent(s);  
                   amino protective group;  
                   heptylnaphthoyl;  
                   hexylnaphthoyl;  
 35               aroyl substituted with heterocyclic carbamoyl which

may have one or more suitable substituent(s);

lower alkanoyl substituted with cyclo(lower)alkyl  
which may have one or more suitable substituent(s);

5 lower alkanoyl substituted with thienyl having  
heterocyclic group which may have one or more suitable  
substituent(s); or

lower alkenoyl substituted with heterocyclic group  
which may have one or more suitable substituent(s),

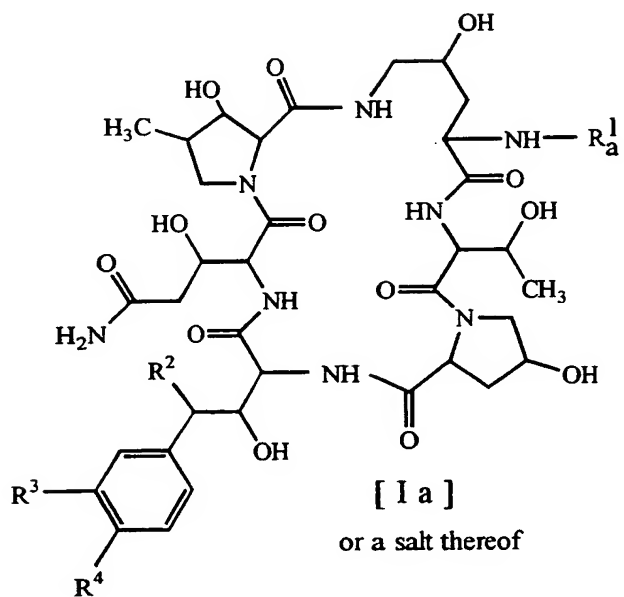
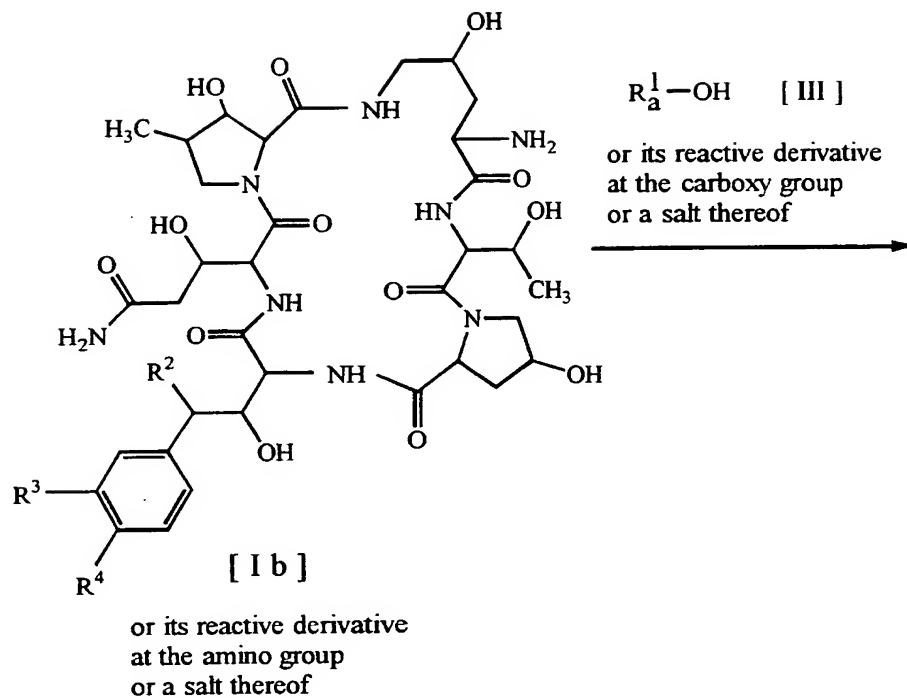
$R^2$  is hydrogen or hydroxy,

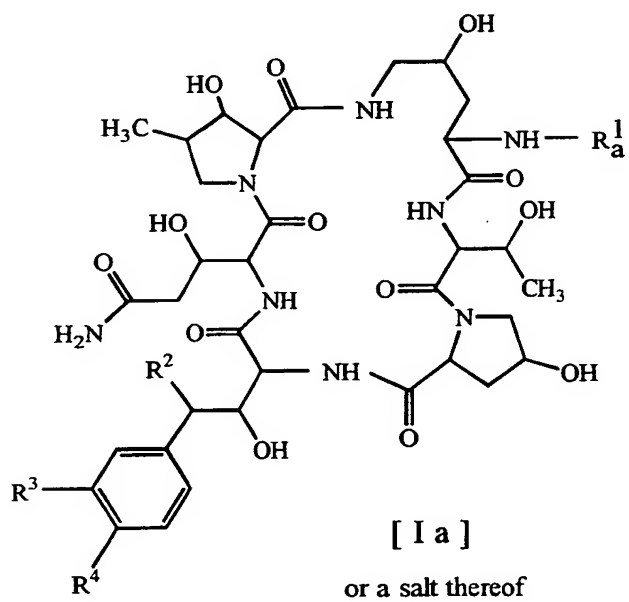
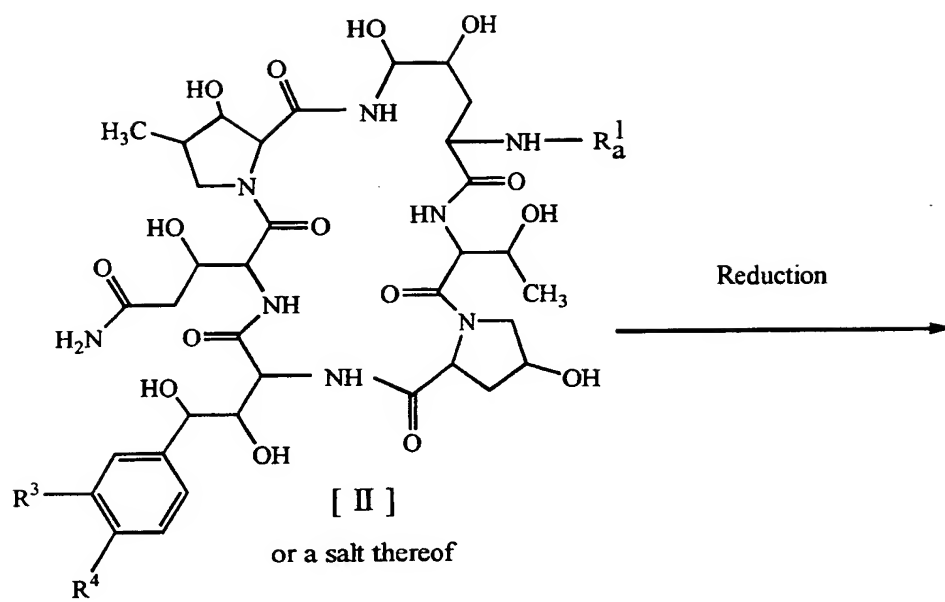
10  $R^3$  is hydroxy, hydroxysulfonyloxy or lower alkoxy, and

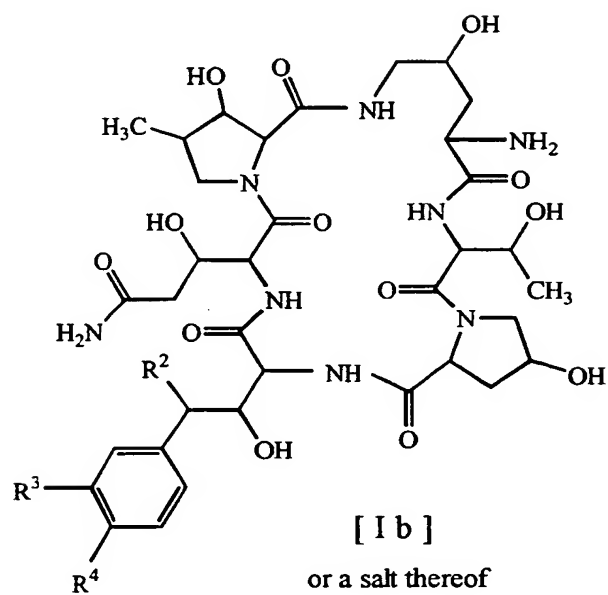
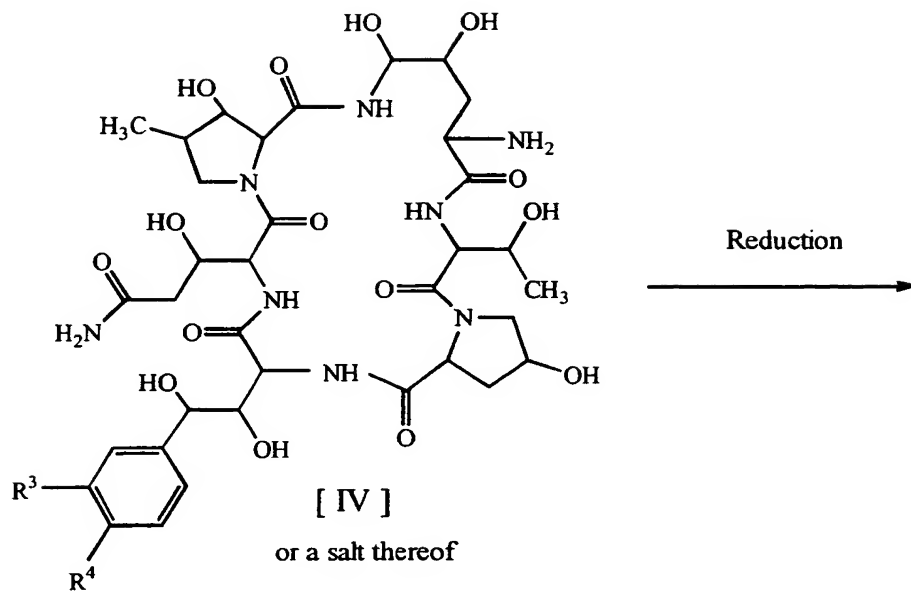
$R^4$  is hydroxy or lower alkoxy,

or a salt thereof.

The new polypeptide compound [I] and a salt thereof can  
be prepared by the process as illustrated in the following  
15 reaction schemes.

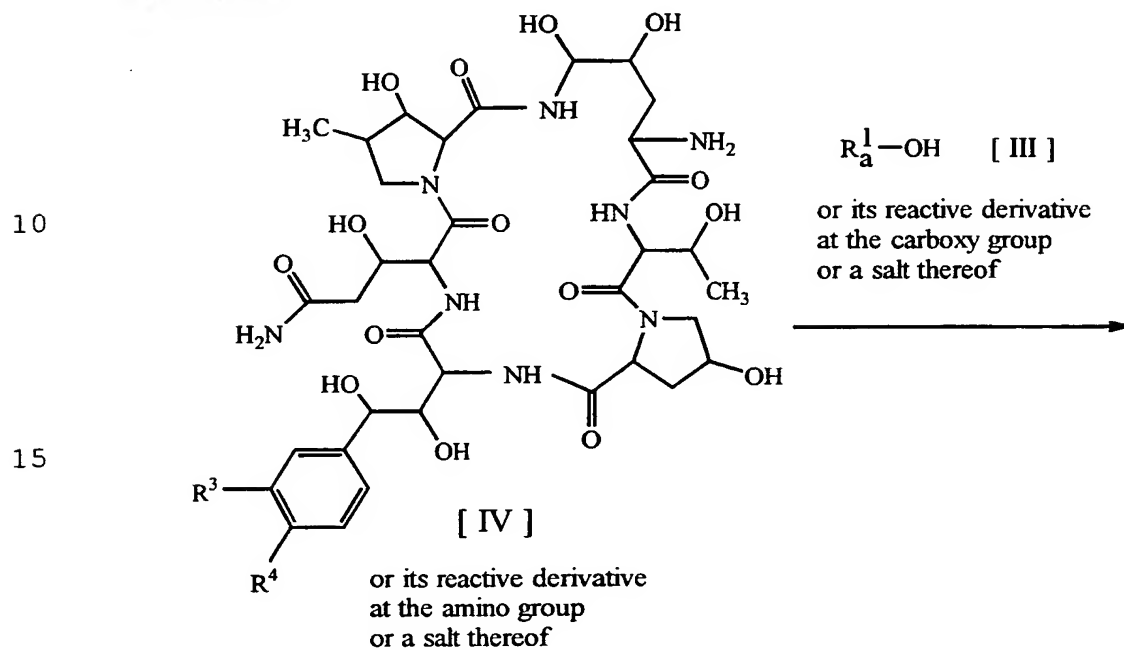
Process 1

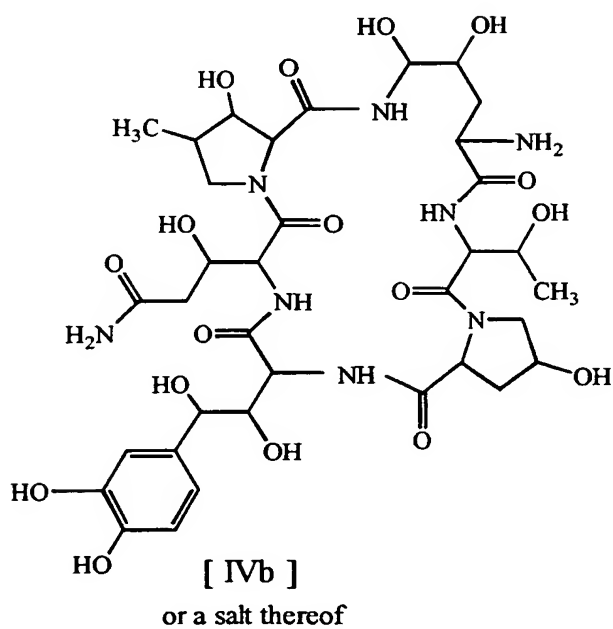
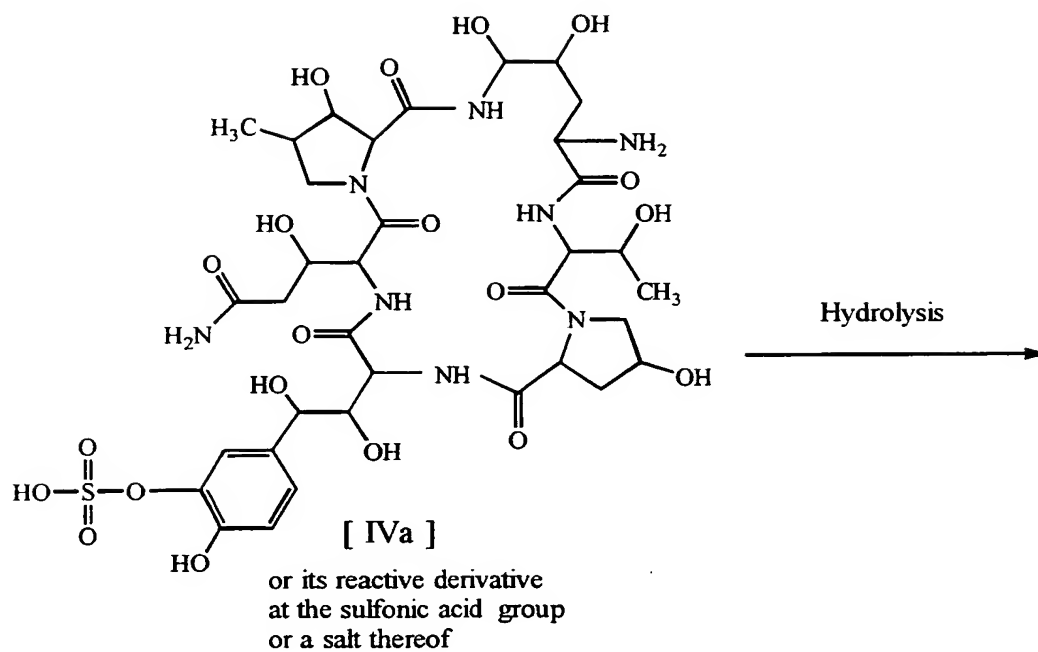
Process 2

Process 3

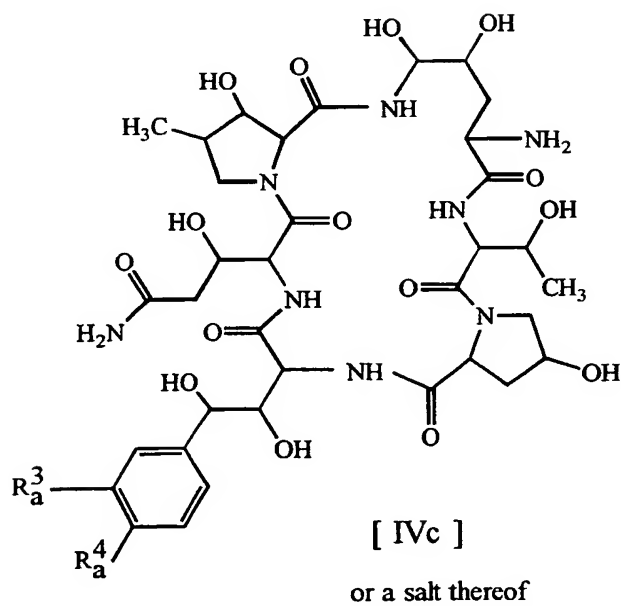
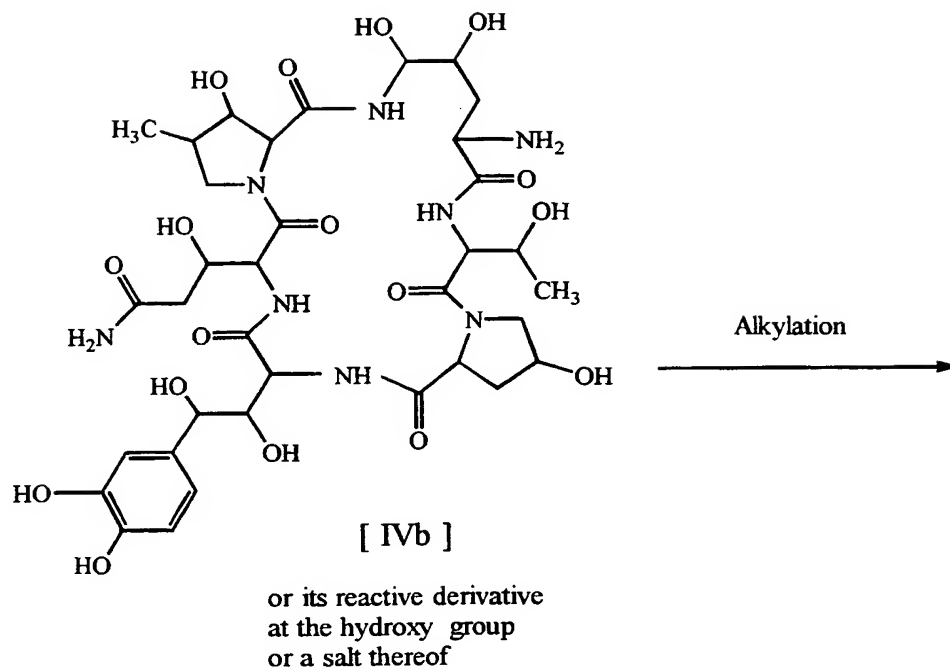
The starting compound [II] and [IV], or a salt thereof can be prepared by the process as illustrated in the following reaction schemes.

5 Process A



Process B



Process C

wherein

$R^2$ ,  $R^3$  and  $R^4$  are as defined above,

$R_a^1$  is arylamino(lower)alkanoyl which may have one or more

suitable substituent(s);

5 aroyl substituted with heterocyclic group which may have one or more suitable substituent(s);

aroyl substituted with aryl having higher alkyl;

aroyl substituted with aryl having lower alkyl;

aryl( $C_2$ - $C_6$ )alkanoyl substituted with aryl having

10 lower alkyl;

lower alkanoyl substituted with unsaturated condensed heterocyclic group which may have one or more suitable substituent(s);

15 lower alkanoyl substituted with pyridyl which may have one or more suitable substituent(s);

amino protective group;

heptylnaphthoyl;

hexylnaphthoyl;

20 aroyl substituted with heterocyclic carbamoyl which may have one or more suitable substituent(s);

lower alkanoyl substituted with cyclo(lower)alkyl which may have one or more suitable substituent(s);

25 lower alkanoyl substituted with thienyl having heterocyclic group which may have one or more suitable substituent(s); or

lower alkenoyl substituted with heterocyclic group which may have one or more suitable substituent(s),

$R_a^3$  is lower alkoxy, and

$R_a^4$  is hydroxy or lower alkoxy.

30 Suitable salt of the new polypeptide compound [I] is a pharmaceutically acceptable and conventional non-toxic salt, and may include a salt with a base or an acid addition salt

such as a salt with an inorganic base, for example, an alkali metal salt (e.g., sodium salt, potassium salt, etc.), an alkaline earth metal salt (e.g., calcium salt, magnesium salt, etc.), an ammonium salt;

5 a salt with an organic base, for example, an organic amine salt (e.g., triethylamine salt, diisopropylethylamine salt, pyridine salt, picoline salt, ethanolamine salt, triethanolamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt, etc.);

10 an inorganic acid addition salt (e.g., hydrochloride, hydrobromide, sulfate, phosphate, etc.);

an organic carboxylic sulfonic acid addition salt (e.g., formate, acetate, trifluoroacetate, maleate, tartrate, fumarate, methanesulfonate, benzenesulfonate,

15 toluenesulfonate, etc.);

a salt with a basic or acidic amino acid (e.g., arginine, aspartic acid, glutamic acid, etc.).

Suitable examples and illustration of the various  
20 definitions in the above and subsequent descriptions of the present specification, which the present invention intends to include within the scope thereof, are explained in detail as follows :

The term "lower" is used to intend a group having 1 to  
25 6 carbon atom(s), unless otherwise provided.

The term "higher" is used to intend a group having 7 to 20 carbon atoms, unless otherwise provided.

Suitable example of "one or more" may be the number of 1 to 6, in which the preferred one may be the number of 1 to  
30 3.

Suitable example of "lower alkanoyl" may include straight or branched one such as formyl, acetyl,  
2-methylacetyl, 2,2-dimethylacetyl, propionyl, butyryl, isobutyryl, pentanoyl, 2,2-dimethylpropionyl, hexanoyl, and  
35 the like.

Suitable example of "suitable substituent(s)" in the  $R^1$  and  $R_a^1$  may include higher alkoxy, aryl which has one or more higher alkoxy, higher alkyl, lower alkyl, aryl which has one or more lower alkoxy, heterocyclic group which may have one or more higher alkoxy, aryl which has one or more cyclo(lower)alkyl, aryl which has one or more lower alkoxy(higher)alkoxy, aryl which has one or more heterocyclic groups, cyclo(lower)alkyl which has one or more cyclo(lower)alkyl, aryl substituted with aryl which may have one or more lower alkoxy, aryl substituted with aryl which may have one more higher alkoxy, aryl substituted with aryl which may have one or more lower alkoxy having heterocyclic group, aryl which has one or more lower alkoxy(lower)alkoxy, heterocyclic group which may have one or more higher alkyl, aryl substituted with aryl which may have one or more aryloxy(lower)alkoxy, aryl substituted with aryl which may have one or more lower alkenyloxy, aryl substituted with aryl which may have one or more lower alkoxy(higher)alkoxy, aryl substituted with aryl which may have one or more heterocyclic(lower)alkoxy, aryl which has one or more aryloxy(lower)alkoxy, heterocyclic group which may have one or more heterocyclic groups, aryl which has one or more cyclo(lower)alkyloxy, aryl which has one or more heterocyclic groups having lower alkoxy, aryl which has one or more heterocyclic groups having cyclo(lower)alkyloxy, aryl which has one or more heterocyclic groups having aryl(lower)alkyloxy, aryl which has one or more heterocyclic groups having cyclo(lower)alkyl, aryl which has one or more heterocyclic groups having aryl, heterocyclic group which may have one or more aryl having lower alkoxy, heterocyclic group which may have one or more aryl having higher alkoxy(lower)alkyl, heterocyclic group which may have one or more aryl having lower alkoxy(lower)alkoxy, heterocyclic group which may have one or more aryl having cyclo(lower)alkyl, heterocyclic group which

may have one or more aryl having heterocyclic group,  
heterocyclic group which may have one or more aryl substituted  
with heterocyclic(lower)alkyl having aryl, heterocyclic group  
which may have one or more heterocyclic groups having aryl,  
5 aryl substituted with aryl which may have one or more  
cyclo(lower)alkyloxy, aryl substituted with aryl which may  
have one or more lower alkoxy(lower)alkyl, aryl substituted  
with aryl which may have one or more lower alkoxy(lower)alkoxy,  
aryl substituted with aryl which may have one or more lower  
10 alkoxy(lower)alkoxy(lower)alkyl, aryl substituted with aryl  
which may have one or more lower  
alkoxy(lower)alkoxy(lower)alkoxy, aryl substituted with aryl  
which may have one or more heterocyclic groups, aryl which has  
one or more cyclo(lower)alkyloxy, aryl which has one or more  
15 lower alkoxy(higher)alkylthio, aryl which has one or more  
lower alkoxy having heterocyclic group, cyclo(lower)alkyl  
which may have one or more lower alkyl, cyclo(lower)alkyl-which  
may have one or more aryl, aryl, and the like.

Suitable example of "lower alkoxy" may include straight  
20 or branched one such as methoxy, ethoxy, propoxy, isopropoxy,  
butoxy, isobutoxy, tert-butoxy, pentyloxy, tert-pentyloxy,  
neo-pentyloxy, hexyloxy, isohexyloxy and the like,  
in which the preferred one may be methoxy, ethoxy, propoxy,  
butoxy, pentyloxy, hexyloxy and isohexyloxy.

25 Suitable example of "higher alkoxy" may include straight  
or branched one such as heptyloxy, octyloxy,  
3,5-dimethyloctyloxy, 3,7-dimethyloctyloxy, nonyloxy,  
decyloxy, undecyloxy, dodecyloxy, tridecyloxy, tetradecyloxy,  
hexadecyloxy, heptadecyloxy, octadecyloxy, nonadecyloxy,  
30 icosyloxy, and the like,  
in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>) alkoxy, and the more  
preferred one may be heptyloxy and octyloxy.

Suitable example of "lower alkyl" may include straight  
or branched one having 1 to 6 carbon atom(s), such as methyl,  
35 ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl,

tert-butyl, pentyl, tert-pentyl, neo-pentyl, hexyl, isohexyl and the like,  
in which the preferred one may be methyl, pentyl, hexyl and isohexyl.

5           Suitable example of "higher alkyl" may include straight or branched one having 7 to 20 carbon atoms, such as heptyl, octyl, 3,5-dimethyloctyl, 3,7-dimethyloctyl, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl, icosyl, and the like,  
10           in which the preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkyl, and the more preferred one may be heptyl, octyl, nonyl and decyl.

          Suitable example of "aryl" and "ar" moiety may include phenyl which may have lower alkyl (e.g., phenyl, mesityl, xylyl, tolyl, etc.), naphthyl, anthryl, indanyl, and the like,  
15           in which the preferred one may be phenyl and naphthyl, and this "aryl" and "ar" moiety may have halogen or lower alkoxy.

          Suitable example of "aroyl" may include benzoyl, toluoyl, naphthoyl, anthrylcarbonyl, and the like,  
in which the preferred one may be benzoyl and naphthoyl, and  
20           this "aroyl" may have lower alkyl.

          Suitable example of "heterocyclic group" and "heterocyclic" moiety may include

          unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 4 nitrogen  
25           atom(s), for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.), tetrazolyl (e.g., 1H-tetrazolyl, 2H-tetrazolyl, etc.), etc.;

30           saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 to 4 nitrogen atom(s), for example, pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, etc.;

          unsaturated condensed heterocyclic group containing 1 to  
35           4 nitrogen atom(s), for example, indolyl, isoindolyl,

indoliny, indoliziny, benzimidazolyl, quinoly, isoquinoly, indazolyl, benzotriazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, oxazolyl, isoxazolyl, oxadiazolyl (e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.), etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, morpholiny, sydnony, morpholino, etc.;

unsaturated condensed heterocyclic group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), for example, benzoxazolyl, benzoxadiazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, thiazolyl, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.), dihydrothiaziny, etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example thiazolidiny, thiomorpholiny, thiomorpholino, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing 1 or 2 sulfur atom(s), for example, thienyl, dihydrodithiiny, dihydrodithionyl, etc.;

unsaturated condensed heterocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), for example, benzothiazolyl, benzothiadiazolyl, imidazothiadiazolyl, etc.;

unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, furyl, etc.;

saturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom, for example, tetrahydrofuran, tetrahydropyran, etc.;

5       unsaturated 3 to 8-membered (more preferably 5 or 6-membered) heteromonocyclic group containing an oxygen atom and 1 or 2 sulfur atom(s), for example, dihydrooxathiinyl, etc.;

      unsaturated condensed heterocyclic group containing 1 or 2 sulfur atom(s), for example benzothienyl, benzodithiinyl, etc.;

10       unsaturated condensed heterocyclic group containing an oxygen atom and 1 or 2 sulfur atom(s), for example, benzoxathiinyl, etc.; and the like and this "heterocyclic group" and "heterocyclic" moiety may have lower alkyl or cyclo(lower)alkyl.

15       Suitable example of "lower alkenyloxy" may include vinyloxy, 1-(or 2-)propenyloxy, 1-(or 2- or 3-)butenyloxy, 1-(or 2- or 3- or 4-)pentyloxy, 1-(or 2- or 3- or 4- or 5-)hexenyloxy, and the like, in which the preferred one may be (C<sub>2</sub>-C<sub>6</sub>)alkenyloxy, and the most preferred one may be  
20       2-propenyloxy.

      Suitable example of "cyclo(lower)alkyl" may include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like, in which the preferred one may be cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl, and the most preferred one may be cyclohexyl and this  
25       "cyclo(lower)alkyl" may have lower alkyl.

      Suitable "amino protective group" may include acyl group as explained below, a conventional protective group such as ar(lower)alkyl which may have 1 to 3 suitable substituent(s) (e.g. benzyl, phenethyl, 1-phenylethyl, benzhydryl, trityl,  
30       etc.), [5-(lower)alkyl-2-oxo-1,3-dioxol-4-yl](lower)alkyl [e.g. (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, etc.] or the like; and the like.

      Suitable "acyl group" and "acyl" may include aliphatic acyl, aromatic acyl, arylaliphatic acyl and heterocyclic-  
35       aliphatic acyl derived from carboxylic acid, carbonic acid,



carbamic acid, sulfonic acid, and the like.

Suitable example of said "acyl group" may be illustrated as follows.

- Aliphatic acyl such as lower or higher alkanoyl (e.g.,  
5 formyl, acetyl, propanoyl, butanoyl, 2-methylpropanoyl, pentanoyl, 2,2-dimethylpropanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl, icosanoyl, etc.);  
10 lower or higher alkoxy carbonyl (e.g., methoxy carbonyl, ethoxy carbonyl, t-butoxy carbonyl, t-pentyloxy carbonyl, heptyloxy carbonyl, etc.);  
lower or higher alkylsulfonyl (e.g., methylsulfonyl, ethylsulfonyl, etc.);  
15 lower or higher alkoxy sulfonyl (e.g., methoxy sulfonyl, ethoxy sulfonyl, etc.); or the like;

- Aromatic acyl such as  
aroyl (e.g., benzoyl, toluoyl, naphthoyl, etc.);  
ar(lower)alkanoyl [e.g., phenyl(C<sub>1</sub>-C<sub>6</sub>)alkanoyl (e.g.,  
20 phenylacetyl, phenylpropanoyl, phenylbutanoyl, phenylisobutanoyl, phenylpentanoyl, phenylhexanoyl, etc.), naphthyl(C<sub>1</sub>-C<sub>6</sub>)alkanoyl (e.g., naphthylacetyl, naphthylpropanoyl, naphthylbutanoyl, etc.), etc.];  
ar(lower)alkenoyl [e.g., phenyl(C<sub>3</sub>-C<sub>6</sub>)alkenoyl (e.g.,  
25 phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl, phenylhexenoyl, etc.), naphthyl(C<sub>3</sub>-C<sub>6</sub>)alkenoyl (e.g., naphthylpropenoyl, naphthylbutenoyl, etc.), etc.];  
ar(lower)alkoxy carbonyl [e.g., phenyl(C<sub>1</sub>-C<sub>6</sub>)alkoxy carbonyl  
30 (e.g., benzyloxy carbonyl, etc.), fluorenyl(C<sub>1</sub>-C<sub>6</sub>)alkoxy carbonyl (e.g., fluorenylmethyloxy carbonyl, etc.), etc.];  
aryloxy carbonyl (e.g., phenoxy carbonyl, naphthyloxy carbonyl, etc.);  
aryloxy(lower)alkanoyl (e.g., phenoxyacetyl,  
35 phenoxypropionyl, etc.);

arylcarbamoyl (e.g., phenylcarbamoyl, etc.);  
arylthiocarbamoyl (e.g., phenylthiocarbamoyl, etc.);  
arylglyoxyloyl (e.g., phenylglyoxyloyl, naphthylglyoxyloyl,  
etc.);

- 5 arylsulfonyl which may have 1 to 4 lower alkyl (e.g.,  
phenylsulfonyl, p-tolylsulfonyl, etc.); or the like;

Heterocyclic acyl such as

- heterocycliccarbonyl;  
heterocyclic(lower)alkanoyl (e.g., heterocyclicacetyl,  
10 heterocyclicpropanoyl, heterocyclicbutanoyl,  
heterocyclicpentanoyl, heterocyclichexanoyl, etc.);  
heterocyclic(lower)alkenoyl (e.g., heterocyclicpropenoyl,  
heterocyclicbutenoyl, heterocyclicpentenoyl,  
heterocyclichexenoyl, etc.);

- 15 heterocyclicglyoxyloyl; or the like;  
in which suitable "heterocyclic" moiety in the terms  
"heterocycliccarbonyl", "heterocyclic(lower)alkanoyl",  
heterocyclic(lower)alkenoyl" and "heterocyclicglyoxyloyl"  
can be referred to aforementioned "heterocyclic" moiety, in  
20 which the preferred one may be ar(lower)alkoxycarbonyl, and  
the more preferred one may be phenyl(C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl and  
fluorenyl(C<sub>1</sub>-C<sub>4</sub>)alkoxycarbonyl, and the most preferred one  
may be benzyloxycarbonyl and fluorenylmethyloxycarbonyl.

- 25 Suitable example of "arylamino" moiety in the term of  
"arylamino(lower)alkanoyl which may have one or more suitable  
substituent(s)" may be phenylamino, mesitylamino, tolylamino,  
naphthylamino, anthrylamino, and the like, in which the  
preferred one may be naphthylamino.

- 30 Suitable example of "lower alkanoyl" moiety in the term  
of "arylamino(lower)alkanoyl which may have one or more  
suitable substituent(s)" can be referred to aforementioned  
"lower alkanoyl", in which the preferred one may be formyl.

- 35 Suitable example of "suitable substituent(s)" moiety in  
the term of "arylamino(lower)alkanoyl which may have one or

more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)", in which the preferred one may be higher alkoxy, and the most preferred one may be heptyloxy.

5           Suitable example of "arylamino(lower)alkanoyl which may have one or more suitable substituent(s)" may be naphthylaminocarbonyl having higher alkoxy, in which the preferred one may be naphthylaminocarbonyl having heptyloxy.

10           Suitable example of "aroyl" moiety in the term of "aroyl substituted with heterocyclic group which may have one or more suitable substituent(s)" can be referred to aforementioned "aroyl", in which the preferred one may be benzoyl.

15           Suitable example of "heterocyclic group" moiety in the term of "aroyl substituted with heterocyclic group which may have one or more suitable substituent(s)" can be referred to aforementioned "heterocyclic group", in which the preferred one may be saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), unsaturated 3 to 8-membered  
20           heteromonocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), unsaturated 3 to 8-membered heteromonocyclic group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s) and unsaturated condensed heterocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen  
25           atom(s) and the more preferred one may be piperazinyl, thiadiazolyl, oxadiazolyl, imidazothiadiazolyl and isoxazolyl.

          Suitable example of "suitable substituent(s)" moiety in the term of "aroyl substituted with heterocyclic group which  
30           may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)", in which the preferred one may be aryl which has one or more higher alkoxy, aryl which has one or more lower alkoxy, aryl which has one or more cyclo(lower)alkyl, aryl which has one or more lower  
35           alkoxy(higher)alkoxy, aryl which has one or more heterocyclic

groups, cyclo(lower)alkyl which may have one or more  
cyclo(lower)alkyl, aryl substituted with aryl which may have  
one or more lower alkoxy, aryl substituted with aryl which may  
have one or more higher alkoxy, aryl substituted with aryl which  
5 may have one or more lower alkoxy having heterocyclic group,  
aryl which has one or more lower alkoxy(lower)alkoxy,  
heterocyclic group which may have one or more higher alkyl,  
aryl substituted with aryl which may have one or more  
aryloxy(lower)alkoxy, aryl substituted with aryl which may  
10 have one or more lower alkenyloxy, aryl substituted with aryl  
which may have one or more lower alkoxy(higher)alkoxy, aryl  
substituted with aryl which has one or more  
heterocyclic(lower)alkoxy, in which heterocyclic group may  
have one or more lower alkyl, aryl which has one or more  
15 aryloxy(lower)alkoxy, heterocyclic group which may have one  
or more heterocyclic groups, aryl which has one or more  
cyclo(lower)alkyloxy, aryl which has one or more heterocyclic  
groups having lower alkoxy, aryl which has one or more  
heterocyclic groups having cyclo(lower)alkyloxy, aryl which  
20 has one or more heterocyclic groups having aryl(lower)alkyloxy,  
aryl which has one or more heterocyclic groups having  
cyclo(lower)alkyl, aryl which has one or more heterocyclic  
groups having aryl, heterocyclic group which may have one or  
more aryl having lower alkoxy, heterocyclic group which may  
25 have one or more aryl having higher alkoxy(lower)alkyl,  
heterocyclic group which may have one or more aryl having lower  
alkoxy(lower)alkoxy, heterocyclic group which may have one or  
more aryl having cyclo(lower)alkyl, heterocyclic group which  
may have one or more aryl having heterocyclic group,  
30 heterocyclic group which may have one or more aryl substituted  
with heterocyclic(lower)alkyl having aryl, heterocyclic group  
which may have one or more heterocyclic groups having aryl,  
aryl substituted with aryl which may have one or more  
cyclo(lower)alkyloxy, aryl substituted with aryl which may  
35 have one or more lower alkoxy(lower)alkyl, aryl substituted

with aryl which may have one or more lower alkoxy(lower)alkoxy,  
aryl substituted with aryl which may have one or more lower  
alkoxy(lower)alkoxy(lower)alkyl, aryl substituted with aryl  
which may have one or more lower  
5 alkoxy(lower)alkoxy(lower)alkoxy, aryl substituted with aryl  
which may have one or more heterocyclic groups, aryl which has  
one or more cyclo(lower)alkyloxy, aryl which has one or more  
lower alkoxy(higher)alkylthio, aryl which has one or more  
lower alkoxy having heterocyclic group, cyclo(lower)alkyl  
10 which may have one or more lower alkyl, cyclo(lower)alkyl which  
may have one or more aryl, aryl, in which the preferred one  
may be phenyl having (C<sub>7</sub>-C<sub>14</sub>)alkoxy, phenyl having (C<sub>4</sub>-  
C<sub>6</sub>)alkoxy, phenyl having cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl, phenyl having  
(C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>7</sub>-C<sub>14</sub>)alkoxy, phenyl having saturated 3 to  
15 8-membered heteromonocyclic group containing 1 to 4 nitrogen  
atom(s), cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl having cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl, phenyl  
substituted with phenyl having (C<sub>1</sub>-C<sub>6</sub>)alkoxy, phenyl -  
substituted with phenyl having (C<sub>7</sub>-C<sub>14</sub>)alkoxy, phenyl  
substituted with phenyl which has (C<sub>1</sub>-C<sub>4</sub>)alkoxy having  
20 saturated 3 to 8-membered heteromonocyclic group containing  
1 to 4 nitrogen atom(s), phenyl having (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>4</sub>-  
C<sub>6</sub>)alkoxy, unsaturated 3 to 8-membered heteromonocyclic group  
containing 1 to 4 nitrogen atom(s) having (C<sub>7</sub>-C<sub>14</sub>)alkyl,  
phenyl substituted with phenyl having phenyloxy(C<sub>1</sub>-C<sub>4</sub>)alkoxy,  
25 phenyl substituted with phenyl having (C<sub>3</sub>-C<sub>6</sub>)alkenyloxy,  
phenyl substituted with phenyl having (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>7</sub>-  
C<sub>14</sub>)alkoxy, phenyl substituted with phenyl which has (C<sub>1</sub>-  
C<sub>4</sub>)alkoxy having saturated 3 to 8-membered heteromonocyclic  
group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen  
30 atom(s) having 1 to 4 (C<sub>1</sub>-C<sub>4</sub>)alkyl, phenyl having phenyloxy-  
(C<sub>1</sub>-C<sub>4</sub>)alkoxy, phenyl having (C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>7</sub>-C<sub>14</sub>)alkoxy,  
unsaturated 3 to 8-membered heteromonocyclic group containing  
1 to 4 nitrogen atom(s) having saturated 3 to 8-membered  
heteromonocyclic group containing 1 to 4 nitrogen atom(s),  
35 phenyl having cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyloxy, phenyl which has

saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) having (C<sub>1</sub>-C<sub>4</sub>)alkoxy, phenyl which has saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) having cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyloxy, phenyl which has saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) having phenyl(C<sub>1</sub>-C<sub>4</sub>)-alkyloxy, phenyl which has saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) having cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl, phenyl which has saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) substituted with cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl having di(C<sub>1</sub>-C<sub>4</sub>)alkyl, phenyl which has saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) substituted with cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl having (C<sub>1</sub>-C<sub>4</sub>)alkyl, phenyl which has saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) substituted with (C<sub>1</sub>-C<sub>4</sub>)alkoxy and phenyl having halogen, phenyl which has saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) substituted with phenyl, phenyl which has unsaturated 3 to 8-membered heteromonocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s) substituted with phenyl having (C<sub>1</sub>-C<sub>6</sub>)alkoxy, unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) which has phenyl having (C<sub>1</sub>-C<sub>6</sub>)alkoxy, unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) which has phenyl having (C<sub>7</sub>-C<sub>14</sub>)-alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) which has phenyl having (C<sub>4</sub>-C<sub>6</sub>)alkyl, unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) which has phenyl having saturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s), unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) which has phenyl substituted with (C<sub>1</sub>-C<sub>6</sub>)alkyl having saturated 3 to 8-membered

heteromonocyclic group containing 1 to 4 nitrogen atom(s)  
having phenyl, unsaturated 3 to 8-membered heteromonocyclic  
group containing 1 to 4 nitrogen atom(s) which has saturated  
3 to 8-membered heteromonocyclic group containing 1 to 4  
5 nitrogen atom(s) having phenyl, phenyl substituted with phenyl  
which has cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyloxy, phenyl substituted with  
phenyl which has (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl  
substituted with phenyl which has (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkoxy,  
phenyl substituted with phenyl which has (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-  
10 C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl substituted with phenyl which  
has (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkoxy, phenyl  
substituted with phenyl which has saturated 3 to 8-membered  
heteromonocyclic group containing 1 to 4 nitrogen atom(s)  
having cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl, phenyl substituted with phenyl  
15 which has saturated 3 to 8-membered heteromonocyclic group  
containing 1 to 4 nitrogen atom(s) substituted with  
cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl having di(C<sub>1</sub>-C<sub>4</sub>)alkyl, phenyl which has  
cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyloxy, phenyl which has (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>7</sub>-  
C<sub>14</sub>)alkylthio, phenyl which has (C<sub>1</sub>-C<sub>6</sub>)alkoxy having  
20 saturated 3 to 8-membered heteromonocyclic group containing  
1 to 4 nitrogen atom(s), phenyl which has (C<sub>1</sub>-C<sub>6</sub>)alkoxy having  
saturated 3 to 8-membered heteromonocyclic group containing  
1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), phenyl which  
has (C<sub>1</sub>-C<sub>6</sub>)alkoxy having saturated 3 to 8-membered  
25 heteromonocyclic group containing 1 or 2 oxygen atom(s) and  
1 to 3 nitrogen atom(s) having di(C<sub>1</sub>-C<sub>4</sub>)alkyl, phenyl which  
has (C<sub>1</sub>-C<sub>6</sub>)alkoxy having saturated 3 to 8-membered  
heteromonocyclic group containing 1 or 2 sulfur atom(s) and  
1 to 3 nitrogen atom(s), cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl which has (C<sub>1</sub>-  
30 C<sub>6</sub>)alkyl, cyclo(C<sub>4</sub>-C<sub>6</sub>)alkyl which has phenyl, indanyl, phenyl  
substituted with saturated 3 to 8-membered heteromonocyclic  
group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s),  
phenyl substituted with saturated 3 to 8-membered  
heteromonocyclic group containing 1 to 4 nitrogen atom(s)  
35 having (C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl substituted with saturated 3 to

8-membered heteromonocyclic group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s) having di(C<sub>1</sub>-C<sub>4</sub>)alkyl, and phenyl substituted with saturated 3 to 8-membered heteromonocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), and the most preferred one may be phenyl having octyloxy, phenyl having hexyloxy, phenyl having cyclohexyl, phenyl having piperidyl, cyclohexyl having cyclohexyl, phenyl having methoxyoctyloxy, phenyl having methoxyheptyloxy, phenyl having butoxy, phenyl having pentyloxy, phenyl substituted with phenyl having methoxy, phenyl substituted with phenyl having propyloxy, phenyl substituted with phenyl having butoxy, phenyl substituted with phenyl having pentyloxy, phenyl substituted with phenyl having hexyloxy, phenyl substituted with phenyl having heptyloxy, phenyl substituted with phenyl which has propyloxy having piperidyl, phenyl having methoxyhexyloxy, isoxazolyl having decyloxy, phenyl substituted with phenyl having phenyloxypropyloxy, phenyl substituted with phenyl having propenyloxy, phenyl substituted with phenyl having phenyloxybutoxy, phenyl substituted with phenyl having methoxyoctyloxy, phenyl substituted with phenyl which has propoxy having dimethyl, phenyl having phenyloxypropoxy, phenyl having phenyloxybutoxy, phenyl having phenyloxypropyloxy, phenyl having methoxypropyloxy, phenyl having methoxyheptyloxy, pyridyl having piperidyl, phenyl having cyclohexyloxy, phenyl which has piperidyl having propoxy, phenyl which has piperidyl having cyclohexyl, phenyl which has piperidyl having phenylmethoxy, phenyl which has piperazinyl having cyclohexyl, phenyl which has piperazinyl substituted with cyclohexyl having dimethyl, phenyl which has piperazinyl substituted with cyclohexyl having methyl, phenyl which has piperidyl substituted with methoxy and chlorophenyl, phenyl which has piperidyl substituted with phenyl, phenyl which has piperazinyl substituted with phenyl, phenyl which has thiadiazolyl substituted with pentyloxyphenyl, pyrazolyl



which has hexyloxyphenyl, pyrazolyl which has  
heptyloxymethylphenyl, piperazinyl which has phenyl having  
cyclohexyl, pyrazolyl which has phenyl having piperidyl,  
pyrazolyl which has phenyl having pyrrolidinyl, pyrazolyl  
5 which has phenyl substituted with piperazinylmethyl having  
phenyl, pyridyl which has piperidyl having phenyl, phenyl  
substituted with phenyl which has cyclohexyloxy, phenyl  
substituted with phenyl which has ethoxymethyl, phenyl  
substituted with phenyl which has ethoxypropoxy, phenyl  
10 substituted with phenyl which has ethoxyethoxy, phenyl  
substituted with phenyl which has methoxypropoxy, phenyl  
substituted with phenyl which has methoxyethoxy, phenyl  
substituted with phenyl which has methoxypentyloxy, phenyl  
substituted with phenyl which has methoxyethoxymethyl, phenyl  
15 substituted with phenyl which has methoxyethoxyethoxy, phenyl  
substituted with phenyl which has piperazinyl having  
cyclohexyl, phenyl substituted with phenyl which has  
morpholinyl having dimethyl, phenyl which has cyclohexyloxy,  
phenyl which has methoxyheptylthio, phenyl which has  
20 piperidinobutoxy, phenyl which has piperidinopentyloxy,  
phenyl which has piperidinohexyloxy, phenyl which has  
morpholinopentyloxy, phenyl which has morpholinopentyloxy  
having dimethyl, phenyl which has morpholinohexyloxy having  
dimethyl, phenyl which has thiomorpholinopentyloxy,  
25 cyclohexyl which has pentyl, cyclohexyl which has phenyl,  
indanyl, phenyl having piperidyl, phenyl having morpholinyl,  
phenyl having thiomorpholino, phenyl substituted with phenyl  
having methoxybutoxy, phenyl substituted with piperazinyl  
having ethyl, and phenyl substituted with morpholinyl having  
30 dimethyl.

Suitable example of "aroyl substituted with heterocyclic  
group which may have one or more suitable substituent(s)" may  
be benzoyl substituted with piperazinyl which has phenyl  
having octyloxy, benzoyl substituted with piperazinyl which  
35 has phenyl having hexyloxy, benzoyl substituted with

thiadiazolyl which has phenyl having hexyloxy, benzoyl substituted with oxadiazolyl which has phenyl having hexyloxy, benzoyl substituted with piperazinyl which has phenyl having cyclohexyl, benzoyl substituted with thiadiazolyl which has phenyl having methoxyoctyloxy, benzoyl substituted with thiadiazolyl which has phenyl having piperidyl, benzoyl substituted with piperazinyl which has cyclohexyl having cyclohexyl, benzoyl substituted with piperazinyl which has phenyl having methoxyoctyloxy, benzoyl substituted with piperazinyl which has phenyl having methoxyheptyloxy, benzoyl substituted with imidazothiadiazolyl which has phenyl having butyloxy, benzoyl substituted with imidazothiadiazolyl which has phenyl having pentyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having methoxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having propyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having butyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having pentyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having hexyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having heptyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl which has propyloxy having piperidyl, benzoyl substituted with thiadiazolyl which has phenyl having methoxyhexyloxy, benzoyl substituted with oxadiazolyl which has pyrazolyl having decyl, benzoyl substituted with thiadiazolyl which has pyrazolyl having decyl, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having phenyloxypropyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having propenyloxy, benzoyl substituted with thiadiazolyl which has phenyl having methoxyhexyloxy, benzoyl substituted with oxadiazolyl which has phenyl substituted with phenyl having phenyloxybutyloxy, benzoyl substituted with oxadiazolyl which

has phenyl substituted with phenyl having methoxyoctyloxy,  
benzoyl substituted with oxadiazolyl which has phenyl  
substituted with phenyl which has propyloxy having  
dimethylmorpholinyl, benzoyl substituted with thiadiazolyl  
5 which has phenyl having phenyloxybutyloxy, benzoyl  
substituted with thiadiazolyl which has phenyl having  
phenyloxypropyloxy, benzoyl substituted with thiadiazolyl  
which has phenyl having phenyloxypropyloxy, benzoyl  
substituted with thiadiazolyl which has phenyl having  
10 methoxypropyloxy, benzoyl substituted with thiadiazolyl which  
has phenyl having methoxyheptyloxy, benzoyl substituted with  
thiadiazolyl which has pyridyl having piperidyl, benzoyl  
substituted with imidazothiadiazolyl which has phenyl having  
propyloxy, benzoyl substituted with imidazothiadiazolyl which  
15 has phenyl having cyclohexyloxy, benzoyl substituted with  
isoxazolyl which has phenyl having propyloxy, benzoyl  
substituted with thiadiazolyl having phenyl which has  
piperidyl having propoxy, benzoyl substituted with  
thiadiazolyl having phenyl which has piperidyl having  
20 cyclohexyloxy, benzoyl substituted with thiadiazolyl having  
phenyl which has piperidyl having phenylmethoxy, benzoyl  
substituted with imidazothiadiazolyl having phenyl which has  
piperazinyl having cyclohexyl, benzoyl substituted with  
thiadiazolyl having phenyl which has piperazinyl substituted  
25 with cyclohexyl having dimethyl, benzoyl substituted with  
thiadiazolyl having phenyl which has piperazinyl having  
cyclohexyl, benzoyl substituted with thiadiazolyl having  
phenyl which has piperazinyl substituted with cyclohexyl  
having methyl, benzoyl substituted with thiadiazolyl having  
30 phenyl which has piperidyl substituted with methoxy and  
chlorophenyl, benzoyl substituted with thiadiazolyl having  
phenyl which has piperidyl substituted with phenyl, benzoyl  
substituted with thiadiazolyl having phenyl which has  
piperazinyl substituted with phenyl, benzoyl substituted with  
35 thiadiazolyl having phenyl which has thiadiazolyl substituted

with pentyloxyphenyl, benzoyl substituted with thiadiazolyl  
having pyrazolyl which has hexyloxyphenyl, benzoyl  
substituted with thiadiazolyl having pyrazolyl which has  
heptyloxymethylphenyl, benzoyl substituted with piperidyl  
5 having piperazinyl which has phenyl having cyclohexyl, benzoyl  
substituted with thiadiazolyl having pyrazolyl which has  
phenyl having piperidyl, benzoyl substituted with  
thiadiazolyl having pyrazolyl which has phenyl having  
pyrrolidinyl, benzoyl substituted with thiadiazolyl having  
10 pyrazolyl which has phenyl substituted with piperazinylmethyl  
having phenyl, benzoyl substituted with thiadiazolyl having  
pyridyl which has piperidyl having phenyl, benzoyl substituted  
with thiadiazolyl having phenyl substituted with phenyl which  
has cyclohexyloxy, benzoyl substituted with thiadiazolyl  
15 having phenyl substituted with phenyl which has ethoxymethyl,  
benzoyl substituted with thiadiazolyl having phenyl  
substituted with phenyl which has ethoxypropoxy, benzoyl  
substituted with thiadiazolyl having phenyl substituted with  
phenyl which has ethoxyethoxy, benzoyl substituted with  
20 thiadiazolyl having phenyl substituted with phenyl which has  
methoxypropoxy, benzoyl substituted with thiadiazolyl having  
phenyl substituted with phenyl which has methoxyethoxy,  
benzoyl substituted with piperazinyl having phenyl  
substituted with phenyl which has methoxypentyloxy, benzoyl  
25 substituted with thiadiazolyl having phenyl substituted with  
phenyl which has methoxyethoxymethyl, benzoyl substituted  
with thiadiazolyl having phenyl substituted with phenyl which  
has methoxyethoxyethoxy, benzoyl substituted with  
thiadiazolyl having phenyl substituted with phenyl which has  
30 piperazinyl having cyclohexyl, benzoyl substituted with  
thiadiazolyl having phenyl substituted with phenyl which has  
morpholinyl having dimethyl, benzoyl substituted with  
oxadiazolyl which has phenyl having cyclohexyloxy, benzoyl  
substituted with thiadiazolyl which has phenyl having  
35 cyclohexyloxy, benzoyl substituted with piperazinyl which has

phenyl having cyclohexyloxy, benzoyl substituted with  
piperazinyl which has phenyl having methoxyheptylthio,  
benzoyl substituted with imidazothiadiazolyl which has phenyl  
having piperidinobutoxy, benzoyl substituted with  
5 imidazothiadiazolyl which has phenyl having  
piperidinopentyloxy, benzoyl substituted with  
imidazothiadiazolyl which has phenyl having  
piperidinohexyloxy, benzoyl substituted with  
imidazothiadiazolyl which has phenyl having  
10 morpholinopentyloxy, benzoyl substituted with  
imidazothiadiazolyl having phenyl which has  
morpholinopentyloxy having dimethyl, benzoyl substituted with  
imidazothiadiazolyl having phenyl which has  
morpholinohexyloxy having dimethyl, benzoyl substituted with  
15 imidazothiadiazolyl having phenyl which has  
thiomorpholinopentyloxy, benzoyl substituted with  
piperazinyl which has cyclohexyl having pentyl, benzoyl  
substituted with piperazinyl which has cyclohexyl having  
phenyl, benzoyl substituted with piperazinyl which has indanyl,  
20 benzoyl substituted with imidazothiadiazolyl having phenyl  
which has piperazinyl having ethyl, benzoyl substituted with  
imidazothiadiazolyl which has phenyl having butoxy, benzoyl  
substituted with imidazothiadiazolyl which has phenyl having  
methoxypentyloxy, benzoyl substituted with piperazinyl which  
25 has phenyl having cyclohexyl, dimethylbenzoyl substituted  
with thiadiazolyl which has phenyl having methoxyhexyloxy,  
naphthoyl substituted with oxadiazolyl having phenyl  
substituted with phenyl having butoxy, naphthoyl substituted  
with thiadiazolyl which has phenyl having methoxyhexyloxy,  
30 benzoyl substituted with thiazolyl which has phenyl having  
pentyloxy, benzoyl substituted with thiazolyl which has phenyl  
having hexyloxy, benzoyl substituted with thiazolyl which has  
phenyl having heptyloxy, benzoyl substituted with thiazolyl  
having phenyl substituted with phenyl having propoxy, benzoyl  
35 substituted with imidazothiadiazolyl which has phenyl having

methoxyhexyloxy, benzoyl substituted with  
imidazothiadiazolyl which has phenyl having methoxyheptyloxy,  
benzoyl substituted with imidazothiadiazolyl which has phenyl  
having methoxyoctyloxy, benzoyl substituted with  
5 imidazothiadiazolyl which has phenyl having morpholino,  
benzoyl substituted with imidazothiadiazolyl which has phenyl  
having dimethylmorpholino, benzoyl substituted with  
imidazothiadiazolyl which has phenyl having thiomorpholino,  
benzoyl substituted with imidazothiadiazolyl which has phenyl  
10 having pentyloxy, benzoyl substituted with  
imidazothiadiazolyl which has phenyl having hexyloxy, benzoyl  
substituted with thiadiazolyl which has phenyl having  
cyclohexyl, benzoyl substituted with oxadiazolyl which has  
phenyl having cyclohexyl, benzoyl substituted with  
15 thiadiazolyl which has phenyl substituted with phenyl having  
propoxy, benzoyl substituted with thiadiazolyl which has  
phenyl substituted with phenyl having ethoxy, benzoyl  
substituted with thiadiazolyl which has phenyl substituted  
with phenyl having methoxybutoxy, and benzoyl substituted with  
20 thiadiazolyl which has phenyl substituted with phenyl having  
butoxy.

Suitable example of "aroyl" moiety in the term of "aroyl  
substituted with aryl having higher alkyl" can be referred to  
25 aforementioned "aroyl", in which the preferred one may be  
benzoyl.

Suitable example of "aryl" moiety in the term of "aroyl  
substituted with aryl having higher alkyl" can be referred to  
aforementioned "aryl", in which the preferred one may be  
30 phenyl.

Suitable example of "higher alkyl" moiety in the term of  
"aroyl substituted with aryl having higher alkyl" can be  
referred to aforementioned "higher alkyl", in which the  
preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkyl, and the more preferred one  
35 may be heptyl.

Suitable example of "aroyl substituted with aryl having higher alkyl" may be benzoyl substituted with phenyl having (C<sub>7</sub>-C<sub>14</sub>)alkyl, in which the preferred one may be benzoyl substituted with phenyl having heptyl.

5

Suitable example of "aroyl" moiety in the term of "aroyl substituted with aryl having lower alkyl" can be referred to aforementioned "aroyl", in which the preferred one may be benzoyl.

10

Suitable example of "aryl" moiety in the term of "aroyl substituted with aryl having lower alkyl" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

15

Suitable example of "lower alkyl" moiety in the term of "aroyl substituted with aryl having lower alkyl" can be referred to aforementioned "lower alkyl", in which the preferred one may be (C<sub>4</sub>-C<sub>6</sub>)alkyl, and the more preferred one may be hexyl.

20

Suitable example of "aroyl substituted with aryl having lower alkyl" may be benzoyl substituted with phenyl having (C<sub>4</sub>-C<sub>6</sub>)alkyl, in which the preferred one may be benzoyl substituted with phenyl having hexyl.

25

Suitable example of "aryl" moiety in the term of "aryl(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having lower alkyl" can be referred to aforementioned "aryl", in which the preferred one may be phenyl.

30

Suitable example of "(C<sub>2</sub>-C<sub>6</sub>)alkanoyl" moiety in the term of "aryl(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having lower alkyl" may be acetyl, propionyl, butyryl, etc., in which the preferred one may be (C<sub>2</sub>-C<sub>4</sub>)alkanoyl, and the more preferred one may be propionyl.

35

Suitable example of "lower alkyl" moiety in the term of "aryl(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having lower alkyl" can be referred to aforementioned "lower alkyl", in

which the preferred one may be (C<sub>4</sub>-C<sub>6</sub>)alkyl, and the more preferred one may be pentyl.

Suitable example of "aryl(C<sub>2</sub>-C<sub>6</sub>)alkanoyl substituted with aryl having lower alkyl" may be phenylpropionyl  
5 substituted with phenyl having pentyl.

Suitable example of "lower alkanoyl" moiety in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group which may have one or more suitable  
10 substituent(s)" can be referred to aforementioned "lower alkanoyl", in which the preferred one may be (C<sub>1</sub>-C<sub>3</sub>)alkanoyl, and the more preferred one may be formyl.

Suitable example of "unsaturated condensed heterocyclic group" moiety in the term of "lower alkanoyl substituted with  
15 unsaturated condensed heterocyclic group which may have one or more suitable substituent(s)" can be referred to aforementioned "heterocyclic group", in which the preferred one may be unsaturated condensed heterocyclic group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), and the more  
20 preferred one may be benzoxazolyl.

Suitable example of "suitable substituent(s)" moiety in the term of "lower alkanoyl substituted with unsaturated condensed heterocyclic group which may have one or more  
25 suitable substituent(s)" may be heterocyclic group which may have one or more higher alkoxy and aryl which may have one or more lower alkoxy, in which the preferred one may be unsaturated 3 to 8-membered heteromonocyclic group containing 1 to 4 nitrogen atom(s) having (C<sub>7</sub>-C<sub>14</sub>)alkoxy and phenyl having (C<sub>4</sub>-C<sub>6</sub>)alkoxy, and the more preferred one may be pyridyl having  
30 octyloxy and phenyl having hexyloxy.

Suitable example of "lower alkanoyl substituted with unsaturated condensed heterocyclic group which may have one or more suitable substituent(s)" may be benzoxazolylcarbonyl which has pyridyl having (C<sub>7</sub>-C<sub>14</sub>)alkoxy and  
35 benzoxazolylcarbonyl which has phenyl having (C<sub>4</sub>-C<sub>6</sub>)alkoxy,



in which the preferred one may be benzoxazolylcarbonyl which has pyridyl having octyloxy and benzoxazolylcarbonyl which has phenyl having hexyloxy.

5           Suitable example of "lower alkanoyl" moiety in the term of "lower alkanoyl substituted with pyridyl which may have one or more suitable substituent(s)" can be referred to aforementioned "lower alkanoyl", in which the preferred one may be (C<sub>1</sub>-C<sub>3</sub>)alkanoyl, and the more preferred one may be  
10   formyl.

          Suitable example of "suitable substituent(s)" moiety in the term of "lower alkanoyl substituted with pyridyl which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)", in which the  
15   preferred one may be higher alkoxy, and the more preferred one may be (C<sub>7</sub>-C<sub>14</sub>)alkoxy, and the most preferred one may be heptyloxy and octyloxy.

          Suitable example of "lower alkanoyl substituted with pyridyl which may have one or more suitable substituent(s)"  
20   may be pyridylcarbonyl having (C<sub>7</sub>-C<sub>14</sub>)alkoxy, in which the preferred one may be pyridylcarbonyl having octyloxy and pyridylcarbonyl having heptyloxy.

          Suitable example of "aroyl" moiety in the term of "aroyl  
25   substituted with heterocyclic carbamoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "aroyl", in which the preferred one may be benzoyl.

          Suitable example of "heterocyclic" moiety in the term of  
30   "aroyl substituted with heterocyclic carbamoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "heterocyclic" moiety, in which the preferred one may be unsaturated 3 to 8-membered heteromonocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s),  
35   and the more preferred one may be thiadiazolyl.

Suitable example of "suitable substituent(s)" moiety in the term of "aryl substituted with heterocyclic carbamoyl which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)", in  
5 which the preferred one may be phenyl having (C<sub>1</sub>-C<sub>6</sub>)alkoxy, and the more preferred one may be phenyl having pentyloxy.

Suitable example of "aryl substituted with heterocyclic carbamoyl which may have one or more suitable substituent(s)" may be benzoyl substituted with thiadiazolyl carbamoyl which  
10 has phenyl having pentyloxy.

Suitable example of "lower alkanoyl" moiety in the term of "lower alkanoyl substituted with cyclo(lower)alkyl which may have one or more suitable substituent(s)" can be referred  
15 to aforementioned "lower alkanoyl", in which the preferred one may be formyl.

Suitable example of "cyclo(lower)alkyl" moiety in the term of "lower alkanoyl substituted with cyclo(lower)alkyl which may have one or more suitable substituent(s)" can be  
20 referred to aforementioned "cyclo(lower)alkyl", in which the preferred one may be cyclohexyl.

Suitable example of "suitable substituent(s)" moiety in the term of "lower alkanoyl substituted with cyclo(lower)alkyl which may have one or more suitable substituent(s)" can be  
25 referred to aforementioned "suitable substituent(s)", in which the preferred one may be heterocyclic group which may have one or more aryl having lower alkoxy(lower)alkoxy, and the more preferred one may be thiadiazolyl which has phenyl having methoxyhexyloxy.

30

Suitable example of "lower alkanoyl" moiety in the term of "lower alkanoyl substituted with thienyl having heterocyclic group which may have one or more suitable  
35 substituent(s)" can be referred to aforementioned "lower alkanoyl", in which the preferred one may be formyl.

Suitable example of "heterocyclic group" moiety in the term of "lower alkanoyl substituted with thienyl having heterocyclic group which may have one or more suitable substituent(s)" can be referred to aforementioned

5 "heterocyclic group", in which the preferred one may be unsaturated 3 to 8-membered heteromonocyclic group containing 1 or 2 oxygen atom(s) and 1 to 3 nitrogen atom(s), and the more preferred one may be oxadiazolyl.

Suitable example of "suitable substituent(s)" moiety in

10 the term of "lower alkanoyl substituted with thienyl having heterocyclic group which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)", in which the preferred one may be aryl substituted with aryl which may have one or more lower alkoxy,

15 and the more preferred one may be phenyl substituted with phenyl having pentyloxy.

Suitable example of "lower alkenoyl" moiety in the term of "lower alkenoyl substituted with heterocyclic group which may have one or more suitable substituent(s)" may be acryloyl,

20 butenoyl, pentenoyl, hexenoyl, 2,4-hexendienoyl, and the like, in which the preferred one may be 2,4-hexenedienoyl.

Suitable example of "heterocyclic group" moiety in the term of "lower alkenoyl substituted with heterocyclic group which may have one or more suitable substituent(s)" can be

25 referred to aforementioned "heterocyclic group" moiety, in which the preferred one may be unsaturated 3 to 8-membered heteromonocyclic group containing 1 or 2 sulfur atom(s) and 1 to 3 nitrogen atom(s), and the more preferred one may be

30 thiadiazolyl.

Suitable example of "suitable substituent(s)" moiety in the term of "lower alkenoyl substituted with heterocyclic group which may have one or more suitable substituent(s)" can be referred to aforementioned "suitable substituent(s)", in

35 which the preferred one may be aryl having lower

alkoxy(lower)alkoxy, and the more preferred one may be phenyl having methoxyhexyloxy.

5 The processes for preparing the object polypeptide compound [I] and the starting compound [II] or a salt thereof of the present invention are explained in detail in the following.

#### Process 1

10 The object polypeptide compound [Ia] or a salt thereof can be prepared by reacting the compound [Ib] or its reactive derivative at the amino group or a salt thereof with the compound [III] or its reactive derivative at the carboxy group or a salt thereof.

15 Suitable reactive derivative at the carboxy group of the compound [III] may include an acid halide, an acid anhydride, an activated amide, an activated ester, and the like. Suitable examples of the reactive derivatives may be an acid chloride; an acid azide; a mixed acid anhydride with an acid such as  
20 substituted phosphoric acid [e.g., dialkylphosphoric acid, phenylphosphoric acid, diphenylphosphoric acid, dibenzylphosphoric acid, halogenated phosphoric acid, etc.], dialkylphosphorous acid, sulfurous acid, thiosulfuric acid, sulfuric acid, sulfonic acid [e.g., methanesulfonic acid,  
25 etc.], aliphatic carboxylic acid [e.g., acetic acid, propionic acid, butyric acid, isobutyric acid, pivalic acid, pentanoic acid, isopentanoic acid, 2-ethylbutyric acid, trichloroacetic acid, etc.]; or aromatic carboxylic acid [e.g., benzoic acid, etc.]; a symmetrical acid anhydride; an activated amide with  
30 imidazole, 4-substituted imidazole, dimethylpyrazole, triazole, tetrazole or 1-hydroxy-1H-benzotriazole; or an activated ester [e.g., cyanomethyl ester, methoxymethyl ester, dimethyliminomethyl  $[(CH_3)_2N^+=CH-]$  ester, vinyl ester, propargyl ester, p-nitrophenyl ester, 2,4-dinitrophenyl ester,

trichlorophenyl ester, pentachloropentyl ester, mesylphenyl ester, phenylazophenyl ester, phenyl thioester, p-nitrophenyl thioester, p-cresyl thioester, carboxymethyl thioester, pyranyl ester, pyridyl ester, piperidyl ester, 8-quinolyl thioester, etc.], or an ester with a N-hydroxy compound [e.g. N,N-dimethylhydroxylamine, 1-hydroxy-2-(1H)-pyridone, N-hydroxysuccinimide, N-hydroxyphthalimide, 1-hydroxy-1H-benzotriazole, etc.], and the like. These reactive derivatives can optionally be selected from them according to the mind of the compound [III] to be used.

Suitable salts of the compound [III] and its reactive derivative can be referred to the ones as exemplified for the object polypeptide compound [I].

The reaction is usually carried out in a conventional solvent such as water, alcohol [e.g., methanol, ethanol, etc.], acetone, dioxane, acetonitrile, chloroform, methylene chloride, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction. These conventional solvent may also be used in a mixture with water.

In this reaction, when the compound [III] is used in a free acid form or its salt form, the reaction is preferably carried out in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide;  
N-cyclohexyl-N'-morpholinoethylcarbodiimide;  
N-cyclohexyl-N'-(4-diethylaminocyclohexyl)carbodiimide;  
N,N'-diethylcarbodiimide; N,N'-diisopropylcarbodiimide;  
N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide;  
N,N-carbonylbis-(2-methylimidazole);  
pentamethyleneketene-N-cyclohexylimine;  
diphenylketene-N-cyclohexylimine, ethoxyacetylene;  
1-alkoxy-2-chloroethylene; trialkyl phosphite;  
ethyl polyphosphate; isopropyl polyphosphate;  
phosphorus oxychloride (phosphoryl chloride);  
phosphorus trichloride; thionyl chloride; oxalyl chloride;

lower alkyl haloformate [e.g., ethyl chloroformate, isopropyl chloroformate, etc.]; triphenylphosphine; 2-ethyl-7-hydroxybenzisoaxazolium salt; 2-ethyl-5-(m-sulphophenyl)isoxazolium hydroxide intramolecular salt; 1-(p-chlorobenzenesulfonyloxy)-6-chloro-1H-benzotriazole; so-called Vilsmeier reagent prepared by the reaction of N,N-dimethylformamide with thionyl chloride, phosgene, trichloromethyl chloroformate, phosphorous oxychloride, methanesulfonyl chloride, etc.; or the like.

The reaction may also be carried out in the presence of an inorganic or organic base such as an alkali metal carbonate, alkali metal bicarbonate, tri(lower)alkylamine, pyridine, di(lower)alkylaminopyridine (e.g., 4-dimethylaminopyridine, etc.), N-(lower)alkylmorpholine, N,N-di(lower)alkylbenzylamine, or the like.

The reaction temperature is not critical, and the reaction is usually carried out under cooling to warming.

#### Process 2

The object compound [I<sub>a</sub>] or a salt thereof can be prepared by reducing a compound [II] or a salt thereof.

Suitable salts of the compounds [I<sub>a</sub>] and [II] may be the same as those exemplified for the compound [I].

The reaction can be carried out in a conventional manner, namely, chemical reduction or catalytic reduction.

Suitable reducing agents to be used in chemical reduction are a combination of metal [e.g. tin, zinc, iron, etc.] or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, hydride transfer reagent such as aluminum hydride compound (e.g. lithium aluminum hydride, lithium hydridetri-t-butoxyaluminate, etc.), borohydride compound (e.g. sodium borohydride, sodium cyanoborohydride, etc.) or the like etc.].

Suitable catalysts to be used in catalytic reduction are

conventional ones such as platinum catalyst [e.g. platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalyst [e.g., spongy palladium, palladium black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalyst [e.g. reduced nickel, nickel oxide, Raney nickel, etc.], cobalt catalyst [e.g. reduced cobalt, Raney cobalt, etc.], iron catalyst [e.g. reduced iron, Raney iron, etc.], copper catalyst [e.g. reduced copper, Raney copper, Ullman copper, etc.] or the like.

The reaction of this process is usually carried out in a solvent such as water, alcohol [e.g. methanol, ethanol, propanol, etc.], acetic acid, diethyl ether, dioxane, tetrahydrofuran, methylene chloride, etc. or a mixture thereof.

The reaction is preferably carried out under somewhat milder conditions such as under cooling to warming.

It is included within the scope of the present invention that "hydroxy" in  $R^2$  may be reduced to "hydrogen" during the reaction.

### Process 3

The object compound [Ib] or a salt thereof can be prepared by reducing the starting compound [IV] or a salt thereof to reduction reaction.

This reaction can be carried out in substantially the same manner as Process 2, and therefore the reaction mode and reaction conditions [e.g. solvent, reaction temperature, etc.] of this reaction are to be referred to those as explained in Process 2.

### Process A

The object compound [II] or a salt thereof can be prepared by reacting the starting compound [IV] or its reactive derivative at the amino group or a salt thereof with the compound [III] or its reactive derivative at the carboxy group

or a salt thereof.

This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction conditions [e.g. solvent, reaction temperature, etc.] of this reaction are to be referred to those as explained in Process 1.

#### Process B

The compound [IVb] or a salt thereof can be prepared by subjecting the compound [IVa] or its reactive derivative at the sulfonic acid group or a salt thereof to hydrolysis reaction of the sulfonic acid group.

The hydrolysis is preferably carried out in the presence of a base or an acid including Lewis acid.

Suitable base may include an inorganic base and an organic base such as an alkali metal [e.g., sodium, potassium, etc.], an alkaline earth metal [e.g., magnesium, calcium, etc.], the hydroxide or carbonate or hydrogencarbonate thereof, trialkylamine [e.g. trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0]-non-5-ene, or the like.

Suitable acid may include an organic acid [e.g., formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.], and an inorganic acid [e.g., hydrochloric acid, hydrobromic acid, sulfuric acid, hydrogen chloride, hydrogen bromide, etc.].

The elimination using Lewis acid such as trihaloacetic acid [e.g., trichloroacetic acid, trifluoroacetic acid, etc.], or the like preferably carried out in the presence of cation trapping agent [e.g., anisole, phenol, etc.].

The reaction is usually carried out in a conventional solvent such as water, alcohol [e.g. methanol, ethanol, isopropyl alcohol, etc.], tetrahydrofuran, dioxane, toluene, methylene chloride, ethylene dichloride, chloroform, N,N-dimethylformamide, N,N-dimethylacetamide or any other organic solvent which do not adversely affect the reaction, or the mixture thereof.



The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

The starting compound [IVa] is known compound. It can be prepared by fermentation and synthetic processes disclosed  
5 in EP 0462531 A2.

#### Process C

The compound [IVc] or a salt thereof can be prepared by subjecting the compound [IVb] or its reactive derivative at the hydroxy group or a salt thereof with the diazo compound  
10 [e.g., diazomethane, phenyldiazomethane, diphenyldiazomethane, trimethylsilyldiazomethane,  $\beta$ -diazopropionic acid etc.] or a salt thereof to alkylation reaction of the hydroxy group.

This reaction is usually carried out in the solvent such as water, alcohol [e.g. methanol, ethanol, etc.], benzene,  
15 N,N-dimethylformamide, tetrahydrofuran, toluene, methylene chloride, ethylene dichloride, chloroform, dioxane, diethyl ether, acetonitrile or any other solvents which do not adversely affect the reaction, or the mixture thereof.

The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

The reaction may be usually carried out in the presence of an acid including Lewis acid.

Suitable acid may include an organic acid [e.g., formic  
25 acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc], and an inorganic acid [e.g., hydrochloric acid, hydrobromic acid, sulfuric acid, hydrogen chloride, hydrogen bromide, zinc halide (e.g., zinc chloride, zinc bromide, etc.), etc.] and the like.

The reaction may be also carried out in the presence of an inorganic or an organic base such as an alkali metal [e.g., sodium, potassium, etc.], an alkali metal hydroxide [e.g., sodium hydroxide, potassium hydroxide, etc.], an alkali metal hydrogencarbonate [e.g., sodium hydrogencarbonate, potassium  
35 hydrogencarbonate, etc.], alkaline metal carbonate [e.g.,

sodium carbonate, potassium carbonate, etc.],  
tri(lower)alkylamine [e.g. trimethylamine, triethylamine,  
diisopropylethylamine, etc.], alkali metal hydride [e.g.,  
sodium hydride, etc.], alkali metal (lower)alkoxide [e.g.,  
5 sodium methoxide, sodium ethoxide, etc.], pyridine, lutidine,  
picoline, dimethylaminopyridine, N-(lower)alkylmorpholine,  
N,N-di(lower)alkylbenzylamine, N,N-di(lower)alkylaniline or  
the like.

When the base, the acid and/or the starting compound are  
10 in liquid, they can be used also as a solvent.

The compounds obtained by the above Processes 1 to 3 and  
Processes A to C can be isolated and purified by a conventional  
method such as pulverization, recrystallization,  
15 column-chromatography, high-performance liquid  
chromatography (HPLC), reprecipitation, desalting resin  
column chromatography, or the like.

The compounds obtained by the above Processes 1 to 3 and  
Processes A to C may be obtained as its hydrate, and its hydrate  
20 is included within the scope of present invention.

It is to be noted that each of the object compound (I)  
may include one or more stereoisomer such as optical isomer(s)  
and geometrical isomer(s) due to asymmetric carbon atom(s) and  
double bond(s) and all such isomers and the mixture thereof  
25 are included within the scope of the present invention.

The object compound (I) or a salt thereof includes  
solvated compound [e.g., enclosure compound (e.g., hydrate,  
etc.)]

The object compound (I) or a salt thereof includes both  
30 its crystal form and non-crystal form.

It should be understood that the compounds in the present  
invention may include the prodrug form.

The patent applications and publications cited herein are  
incorporated by reference.

35 This application is based on application No. PP1728/98

and application No. PP3138/98 filed in Australia, the content of which is incorporated hereinto by reference.

5                   Biological property of the polypeptide  
                  compound [I] of the present invention

In order to show the usefulness of the polypeptide compound [I] of the present invention, the biological data of the representative compound is explained in the following.

10   Test (Antimicrobial activity) :

In vitro antimicrobial activity of the object compound of Example 12 disclosed later was determined by microdilution method as described below.

Test Method :

15           The antifungal susceptibility assays were performed by the microdilution method according to M27-A guidelines recommended by the National Committee for Clinical Laboratory Standards (NCCLS) to determine the MICs of the compounds. RPMI1640 medium with L-glutamine, without sodium bicarbonate,  
20   and buffered with 165 mM morpholinepropanesulfonic acid buffer (pH 7.0) was used as a test medium. Inoculum suspension of  $10^6$  CFU/ml were prepared by a hemocytometric procedure, and diluted to obtain an inoculum size of approximately  $0.5 \times 10^3$  to  $2.5 \times 10^3$  CFU/ml. Microplates were incubated at 35°C  
25   and readings were taken when good growth in the growth control. The MICs were defined as the lowest concentrations at which no visible growth was observed.

Test Result :

30

MIC ( $\mu$ g/ml)

Test compound Test organism	The object compound of <u>Example 12</u>
candida albicans FP-633	0.0625

From the test result, it is realized that the object

polypeptide compound [I] of the present invention has an antimicrobial activity (especially, antifungal activity).

5       The pharmaceutical composition of the present invention can be used in the form of a pharmaceutical preparation, for example, in solid, semisolid or liquid form, which contains the object polypeptide compound [I] or a pharmaceutically acceptable salt thereof, as an active ingredient in admixture with an organic or inorganic carrier or excipient which is  
10       suitable for rectal; pulmonary (nasal or buccal inhalation); ocular; external (topical); oral administration; parenteral (including subcutaneous, intravenous and intramuscular) administrations; insufflation (including aerosols from metered dose inhalator); nebulizer; or dry powder inhalator.

15       The active ingredient may be compounded, for example, with the usual non-toxic, pharmaceutically acceptable carriers in a solid form such as granules, tablets, dragees, pellets, troches, capsules, or suppositories; creams; ointments; aerosols; powders for insufflation;  
20       in a liquid form such as solutions, emulsions, or suspensions for injection; ingestion; eye drops; and any other form suitable for use. And, if necessary, there may be included in the above preparation auxiliary substance such as stabilizing, thickening, wetting, emulsifying and coloring  
25       agents; perfumes or buffer; or any other commonly may be used as additives.

      The object polypeptide compound [I] or a pharmaceutically acceptable salt thereof is/are included in the pharmaceutical composition in an amount sufficient to produce the desired  
30       antimicrobial effect upon the process or condition of diseases.

      For applying the composition to human, it is preferable to apply it by intravenous, intramuscular, pulmonary, oral administration, or insufflation. While the dosage of  
35       therapeutically effective amount of the object polypeptide

compound [I] varies from and also depends upon the age and condition of each individual patient to be treated, in the case of intravenous administration, a daily dose of 0.01-20 mg of the object polypeptide compound [I] per kg weight of human being  
5 in the case of intramuscular administration, a daily dose of 0.1-20 mg of the object polypeptide compound [I] per kg weight of human being, in case of oral administration, a daily dose of 0.5-50 mg of the object polypeptide compound [I] per kg weight of human being is generally given for treating or  
10 preventing infectious diseases.

Especially in case of the treatment of prevention of Pneumocystis carinii infection, the followings are to be noted.

For administration by inhalation, the compounds of the present invention are conveniently delivered in the form of  
15 an aerosol spray presentation from pressurized as powders which may be formulated and the powder compositions may be inhaled with the aid of an insufflation powder inhaler device. The preferred delivery system for inhalation is a metered dose  
20 inhalation aerosol, which may be formulated as a suspension or solution of compound in suitable propellants such as fluorocarbons or hydrocarbons.

Because of desirability to directly treat lung and bronchi, aerosol administration is a preferred method of  
25 administration. Insufflation is also a desirable method, especially where infection may have spread to ears and other body cavities.

Alternatively, parenteral administration may be employed using drip intravenous administration.

30 The following Preparations and Examples are given for the purpose of illustrating the present invention in more detail.

#### Preparation 1

A solution of 4-hydroxybenzoic acid methyl ester (100 g)  
35 and 1,6-dibromohexane (481 g) in N,N-dimethylformamide (500

ml) was treated with potassium carbonate (109 g) then heated at 60°C for 2 hours. After cooling, the mixture was diluted with ethyl acetate (3 L) and washed with water (7 x 1 L). The organic layer was dried over magnesium sulfate, filtered, and  
5 evaporated to give a crude oil. Hexane (~100 ml) was added and the resulting precipitate removed by filtration and discarded and the filtrate loaded onto a silica gel column (2 kg). Elution with hexane, followed by 9:1 hexane-ethyl acetate and 8:1 hexane-ethyl acetate afforded methyl 4-(6-bromo-n-hexyloxy)benzoate (186 g) as a white solid.  
10

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.46-1.55 (4H, m), 1.78-1.97 (4H, m),  
3.38-3.46 (2H, m), 3.88 (3H, s), 4.01 (2H, t,  
J=6.3Hz), 6.90 (2H, d, J=8.9Hz), 7.98 (2H, d,  
J=8.9Hz)

15 MASS (m/z) : 315, 317 (M<sup>+</sup>)

The following compound was obtained in a manner similar to that of Preparation 1.

#### Preparation 2

Methyl 4-(7-bromo-n-heptyloxy)benzoate

20 NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.2-1.6 (6H, m), 1.6-2.0 (4H, m),  
3.53 (2H, t, J=6.7Hz), 3.81 (3H, s), 4.04 (2H, t,  
J=6.4Hz), 7.03 (2H, d, J=8.9Hz), 7.90 (2H, d,  
J=8.9Hz)

MASS (m/z) : 329 (M+1), 331 (M+3)

#### 25 Preparation 3

A solution of methyl 4-(6-bromo-n-hexyloxy)benzoate (186 g) in methanol (1 L) was treated with 28% sodium methoxide in methanol (340 ml) and the solution refluxed for 2 hours. After cooling, the stirred solution was adjusted to pH 2 with  
30 1M-hydrochloric acid then extracted with ethyl acetate. The organic layer was washed with water, dried over magnesium sulfate, filtered and evaporated to give a crude oil. This oil was purified on a silica gel column (2 kg, 9:1 hexane-ethyl acetate elution) to give methyl 4-(6-methoxy-n-hexyloxy)benzoate (127 g) as an oil.  
35

NMR (CDCl<sub>3</sub>, δ) : 1.37-1.68 (6H, m), 1.74-1.88 (2H, m),  
3.33 (3H, s), 3.39 (2H, t, J=6.3Hz), 3.88 (3H, s),  
4.01 (2H, t, J=6.4Hz), 6.90 (2H, d, J=8.9Hz), 7.97  
(2H, d, J=8.9Hz)

5 The following compound was obtained in a manner similar  
to that of Preparation 3.

Preparation 4

Methyl 4-(7-methoxy-n-heptyloxy)benzoate

10 NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.6 (8H, m), 1.6-1.9 (2H, m),  
3.21 (3H, s), 3.29 (2H, t, J=6.4Hz), 3.81 (3H, s),  
4.04 (2H, t, J=6.5Hz), 7.03 (2H, d, J=8.9Hz), 7.90  
(2H, d, J=8.9Hz)

MASS (m/z) : 281 (M+1)

Preparation 5

15 A solution of methyl 4-(6-methoxy-n-hexyloxy)benzoate  
(17.05 g) in 1:1 tetrahydrofuran-methanol (300 ml) was treated  
with hydrazine monohydrate (66 ml) and refluxed for 15 hours  
then cooled to room temperature. The reaction mixture was  
poured into water and the resulting precipitate collected by  
20 filtration, washed thoroughly with water then dried under  
hi-vacuum at 50°C to give 4-(6-methoxy-n-  
hexyloxy)benzohydrazide (15.63 g) as a white solid.

NMR (DMSO-d<sub>6</sub>, δ) : 1.29-1.58 (6H, m), 1.65-1.78 (2H,  
m), 3.21 (3H, s), 3.30 (2H, t, J=6.4Hz), 4.00 (2H,  
25 t, J=6.4Hz), 4.40 (2H, s), 6.96 (2H, d, J=8.8Hz),  
7.78 (2H, d, J=8.8Hz), 9.59 (1H, s)

MASS (m/z) : 267 (M+1)

The following compound was obtained in a manner similar  
to that of Preparation 5.

30 Preparation 6

4-(7-Methoxy-n-heptyloxy)benzohydrazide

NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.6 (8H, m), 1.6-1.9 (2H, m),  
3.21 (3H, s), 3.30 (2H, t, J=6.4Hz), 4.00 (2H, t,  
J=6.4Hz), 4.40 (2H, s), 6.96 (2H, d, J=8.7Hz), 7.78  
35 (2H, d, J=8.9Hz), 9.59 (1H, s)

MASS (m/z) : 281 (M+1)

Preparation 7

A mixture of 4-(6-methoxy-n-hexyloxy)benzohydrazide (106.82 g) and pyridine (162 ml) in tetrahydrofuran (1 L) at 0°-5°C was treated portionwise with 4-methoxycarbonylbenzoyl chloride (83.75 g) over 30 minutes. After a further 1 hour at 0°-5°C, and 2 hours at room temperature, tlc indicated complete reaction and the reaction mixture was poured into water (7 L). The resulting precipitate was collected by filtration, washed thoroughly with water, and dried under hi-vacuum at 50°C to give N-[4-(6-methoxy-n-hexyloxy)-benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine (171.9 g) as a white solid.

NMR (DMSO-d<sub>6</sub>, δ) : 1.40-1.80 (8H, m), 3.22 (3H, s), 3.31 (2H, t, J=6.4Hz), 3.90 (3H, s), 4.05 (2H, t, J=6.3Hz), 7.04 (2H, d, J=8.8Hz), 7.90 (2H, d, J=8.8Hz), 8.03 (2H, d, J=8.6Hz), 8.10 (2H, d, J=8.6Hz), 10.41 (1H, s), 10.64 (1H, s)

The following compound was obtained in a manner similar to that of Preparation 7.

Preparation 8

N-[4-(7-Methoxy-n-heptyloxy)benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine

NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.6 (8H, m), 1.6-1.9 (2H, m), 3.21 (3H, s), 3.30 (2H, t, J=6.4Hz), 3.90 (3H, s), 4.05 (2H, t, J=6.4Hz), 7.04 (2H, d, J=8.8Hz), 7.90 (2H, d, J=8.8Hz), 8.03 (2H, d, J=8.6Hz), 8.10 (2H, d, J=8.6Hz), 10.42 (1H, s), 10.63 (1H, s)

MASS (m/z) : 443 (M+1)

Preparation 9

A mixture of N-[4-(6-methoxy-n-hexyloxy)benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine (193.4 g) and phosphorus pentasulfide (113.34 g) in tetrahydrofuran (2.5 L) was heated to reflux for 1 hour then cooled to room temperature and poured into water (7 L). The resulting precipitate was collected by



filtration, washed thoroughly with water then partially dried. The solid was added to 1:1 CH<sub>3</sub>CN-H<sub>2</sub>O (200 ml), stirred then filtered. This procedure was repeated a further 2 times, and the resulting yellow powder washed thoroughly with  
5 acetonitrile (500 ml x 5) then dried under hi-vacuum at 50°C to give methyl 4-[5-[4-(6-methoxy-n-hexyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoate (179.6 g) as a yellow powder.

NMR (CDCl<sub>3</sub>, δ) : 1.40-1.87 (8H, m), 3.34 (3H, s), 3.40 (2H, t, J=6.2Hz), 3.96 (3H, s), 4.03 (2H, t, J=6.5Hz),  
10 6.99 (2H, d, J=8.8Hz), 7.95 (2H, d, J=8.8Hz), 8.07 (2H, d, J=8.5Hz), 8.16 (2H, d, J=8.5Hz)

The following compound was obtained in a manner similar to that of Preparation 9.

Preparation 10

15 Methyl 4-[5-[4-(7-methoxy-n-heptyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoate

NMR (CDCl<sub>3</sub>, δ) : 1.3-2.0 (10H, m), 3.34 (3H, s), 3.38 (2H, t, J=6.4Hz), 3.96 (3H, s), 4.03 (2H, t, J=6.5Hz),  
20 6.99 (2H, d, J=8.8Hz), 7.95 (2H, d, J=8.8Hz), 8.07 (2H, d, J=8.4Hz), 8.43 (2H, d, J=8.4Hz)

MASS (m/z) : 441 (M+1)

Preparation 11

A mixture of methyl 4-[5-[4-(6-methoxy-n-hexyloxy)-phenyl]-1,3,4-thiadiazol-2-yl]benzoate (179.6 g), sodium  
25 hydroxide (25.3 g), water (250 ml), methanol (1 L), and tetrahydrofuran (750 ml) was heated under refluxing for 1 hour then cooled to room temperature and poured into water (7 L). The pH of the stirred mixture was adjusted to 2.0 with 6N-hydrochloric acid and the precipitate collected by filtration,  
30 washed thoroughly with water, followed by acetonitrile, then dried under hi-vacuum at 50°C to give 4-[5-[4-(6-methoxy-n-hexyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid (167 g) as a yellow powder.

NMR (DMSO-d<sub>6</sub>, δ) : 1.27-1.85 (8H, m), 3.22 (3H, s),  
35 3.32 (2H, t, J=6.4Hz), 4.06 (2H, t, J=6.3Hz), 7.12

(2H, d, J=8.8Hz), 7.97 (2H, d, J=8.7Hz), 8.12 (4H, s), 13.28 (1H, br s)

The following compound was obtained in a manner similar to that of Preparation 11.

5 Preparation 12

4-[5-[4-(7-Methoxy-n-heptyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid

IR (KBr) : 2939.0, 2867.6, 2642.0, 1712.5, 1604.5, 1440.6, 1402.0, 1253.5 cm<sup>-1</sup>

10 MASS (m/z) : 427 (M+1)

Preparation 13

A mixture of 4-[5-[4-(6-methoxy-n-hexyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid (50 g), 1-hydroxybenzotriazole (18 g) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide, hydrochloride (34.86 g) in methylene chloride (1 L) was stirred for 16 hours at room temperature then evaporated under reduced pressure and dried for 1 hour under hi-vacuum. Water (1 L) was added to the residue and the resulting precipitate collected by filtration, washed with water (1 L x 5), acetonitrile (1 L x 5), isopropyl ether (250 ml x 2), then dried under hi-vacuum to give 4-[5-[4-(6-methoxy-n-hexyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester (56.92 g) as a yellow powder.

25 IR (KBr) : 1778 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.44-1.89 (8H, m), 3.35 (3H, s), 3.40 (2H, t, J=6.2Hz), 4.05 (2H, t, J=6.4Hz), 7.01 (2H, d, J=8.8Hz), 7.43-7.63 (3H, m), 7.98 (2H, d, J=8.8Hz), 8.13 (1H, d, J=8.2Hz), 8.24 (2H, d, J=8.5Hz), 8.41 (2H, d, J=8.5Hz)

The following compounds [Preparations 14 and 15] were obtained in a manner similar to that of Preparation 13.

Preparation 14

35 4-[5-[4-(7-Methoxy-n-heptyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 3446.2, 2937.1, 2865.7, 1778.0, 1602.6,  
1253.5  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.3-2.0 (10H, m), 3.34 (3H, s), 3.39  
(2H, t,  $J=6.4\text{Hz}$ ), 4.03 (2H, t,  $J=6.5\text{Hz}$ ), 7.01 (2H,  
5 d,  $J=8.8\text{Hz}$ ), 7.4-7.7 (3H, m), 7.98 (2H, d,  $J=8.8\text{Hz}$ ),  
8.13 (1H, d,  $J=8.2\text{Hz}$ ), 8.24 (2H, d,  $J=8.7\text{Hz}$ ), 8.41  
(2H, d,  $J=8.7\text{Hz}$ )

MASS (m/z) : 544 (M+1)

#### Preparation 15

10 4-[5-(4-Pentyloxyphenyl)isoxazol-3-yl]benzoic acid  
benzotriazol-1-yl ester

#### Preparation 16

To 3-hydroxybenzoic acid methyl ester (25 g) and  
potassium carbonate (25 g) in N,N-dimethylformamide (300 ml)  
15 were added 1-bromopentane (25 ml) and the mixture was stirred  
for 7 hours at 80°C. The reaction mixture was added to a mixture  
of water and ethyl acetate. The organic layer was taken and  
dried over magnesium sulfate. The magnesium sulfate was  
filtered off and the filtrate was evaporated under reduced  
20 pressure to give 3-amyloxybenzoic acid methyl ester (35 g).

IR (KBr) : 2954, 2870, 1724, 1587  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.94 (3H, t,  $J=7.0\text{Hz}$ ), 1.43 (4H, m),  
1.80 (2H, m), 3.91 (3H, s), 3.99 (2H, t,  $J=6.6\text{Hz}$ ),  
7.09 (1H, ddd,  $J=7.8$ , 1.7 and 1.7Hz), 7.32 (1H, t,  
25  $J=7.8\text{Hz}$ ), 7.55 (1H, dd,  $J=1.7$  and 1.1Hz), 7.61 (1H,  
ddd,  $J=7.8$ , 1.7 and 1.1Hz)

MASS (m/z) : 223 (M+1)

#### Preparation 17

To 3-amyloxybenzoic acid methyl ester (35 g) in methanol  
30 (200 ml) was added 1N-sodium hydroxide aqueous solution (200  
ml) and the mixture was stirred for 2 days at room temperature.  
Hydroxy chloride (20 ml) was added to the reaction mixture.  
The precipitate was filtered and washed with water,  
acetonitrile and diisopropyl ether to give 3-amyloxybenzoic  
35 acid (30 mg).

IR (KBr) : 2954, 2848, 2570, 1691, 1600, 1591  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.90 (3H, t,  $J=7.0\text{Hz}$ ), 1.40 (4H, m),  
1.73 (2H, m), 4.00 (2H, t,  $J=6.6\text{Hz}$ ), 7.17 (1H, ddd,  
 $J=7.7$ , 2.6 and  $1.2\text{Hz}$ ), 7.39 (1H, t,  $J=7.7\text{Hz}$ ), 7.42  
5 (1H, dd,  $J=1.5$  and  $1.2\text{Hz}$ ), 7.52 (1H, ddd,  $J=7.7$ , 1.5  
and  $1.2\text{Hz}$ )

MASS ( $m/z$ ) : 209 ( $M+1$ )

#### Preparation 18

To a solution of 1-hydroxybenzotriazole (24 g) and 3-  
10 amyloxybenzoic acid (29.5 g) in dichloromethane (500 ml) was  
added 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide  
hydrochloride (WSCD $\cdot\text{HCl}$ ) (41 g) and the mixture was stirred  
for 5 hours at ambient temperature. The reaction mixture was  
added to water. The organic layer was taken and dried over  
15 magnesium sulfate. Magnesium sulfate was filtered off, and  
the filtrate was evaporated under reduced pressure to give  
3-amyloxybenzoic acid benzotriazol-1-yl ester (42 g).

IR (KBr) : 2956, 2935, 2869, 1788, 1600  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.0\text{Hz}$ ), 1.45 (4H, m),  
20 1.84 (2H, m), 4.05 (2H, t,  $J=6.5\text{Hz}$ ), 7.30 (1H, d,  
 $J=9.4\text{Hz}$ ), 7.43-7.56 (4H, m), 7.74 (1H, t,  $J=2.0\text{Hz}$ ),  
8.10 (1H, d,  $J=8.5\text{Hz}$ ), 8.53 (1H, d,  $J=8.5\text{Hz}$ )

MASS ( $m/z$ ) : 326 ( $M+1$ )

#### Preparation 19

25 To a solution of 4-n-butyloxybenzoic acid  
benzotriazol-1-yl ester (15 g) in  $N,N$ -dimethylformamide (100  
ml) was added thiosemicarbazide (5.27 g) and the mixture was  
stirred for 12 hours at ambient temperature. The reaction  
mixture was pulverized with diisopropyl ether. The  
30 precipitate was collected by filtration to give 1-(4-n-  
butyloxybenzoyl)thiosemicarbazide (11.51 g).

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.93 (3H, t,  $J=7.0\text{Hz}$ ), 1.2-1.5 (2H,  
m), 1.6-1.8 (2H, m), 4.02 (2H, t,  $J=6.5\text{Hz}$ ), 6.98 (2H,  
d,  $J=8.8\text{Hz}$ ), 7.56 (1H, s), 7.83 (1H, s), 7.84 (2H,  
35 d,  $J=8.8\text{Hz}$ ), 9.26 (1H, s), 10.21 (1H, s)

The following compound was obtained in a manner similar to that of Preparation 19.

Preparation 20

1-(3-Amyloxybenzoyl)thiosemicarbazide

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.90 (3H, t,  $J=6.8\text{Hz}$ ), 1.39 (4H, m),  
1.73 (2H, m), 4.01 (2H, t,  $J=6.4\text{Hz}$ ), 7.10 (1H, d,  
 $J=8.0\text{Hz}$ ), 7.30-8.00 (5H, m), 9.33 (1H, s), 10.34 (1H,  
s), 8.53 (1H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 282 (M+1)

10 Preparation 21

To a slurry of 1-(4-n-butyloxybenzoyl)thiosemicarbazide (20 g) in toluene (213.3 ml) at 40°C, was added dropwise over 30 minutes, methanesulfonic acid (6.92 ml). The mixture was stirred under refluxing for 12 hours. After cooling to 10°C,  
15 the sulfonate salt was filtered and dried. The salt was placed in water, the solution was adjusted to pH 9 with 1N sodium hydroxide and extracted with ethyl acetate. The organic layer was separated, washed with brine, dried over magnesium sulfate and evaporated under reduced pressure to give 2-amino-5-  
20 (4-n-butyloxyphenyl)-1,3,4-thiadiazole (4.314 g).

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.94 (3H, t,  $J=7.0\text{Hz}$ ), 1.2-1.6 (2H, m), 1.6-1.9 (2H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 7.00 (2H, d,  $J=8.8\text{Hz}$ ), 7.28 (2H, s), 7.66 (2H, d,  $J=8.8\text{Hz}$ )

The following compound was obtained in a manner similar to that of Preparation 21.

Preparation 22

2-Amino-5-(3-amyloxyphenyl)-1,3,4-thiadiazole

IR (KBr) : 3291.9, 3114.5, 2952.5, 1610.3  $\text{cm}^{-1}$

30 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.90 (3H, t,  $J=7.0\text{Hz}$ ), 1.39 (4H, m), 1.73 (2H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 7.00 (1H, d,  $J=8.5\text{Hz}$ ), 7.25-7.42 (5H, m)

MASS (m/z) : 264 (M+1)

Preparation 23

To a suspension of 2-amino-5-(4-n-butyloxyphenyl)-  
35 1,3,4-thiadiazole (1.5 g) in ethanol (30 ml) was added ethyl

4-bromoacetylbenzoate (1.86 g) and the mixture was stirred under refluxing for 1.5 hours. The reaction mixture was pulverized with ethyl acetate. The precipitate was filtered and dried. To a suspension of the powder in xylene (15 ml) was added trifluoroacetic acid (3 ml) and the mixture was stirred under refluxing for 3 hours. The reaction mixture was pulverized with diisopropyl ether. The precipitate was filtered and dried to give 4-[2-(4-butyloxyphenyl)imidazo-[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester trifluoroacetic acid salt (2.15 g).

IR (KBr) : 1714.4, 1602.6, 1278.6, 1255.4,  
1178.3  $\text{cm}^{-1}$

The following compound was obtained in a manner similar to that of Preparation 23

Preparation 24

4-[2-(3-Amyloxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester - trifluoroacetic acid salt

IR (KBr) : 2869.6, 1704.8, 1573.6, 1278.6  $\text{cm}^{-1}$

MASS (m/z) : 436 (M+1)

Preparation 25

To a solution of 4-[2-(4-butyloxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester trifluoroacetic acid salt (2.05 g) in the mixture of methanol (41 ml) and tetrahydrofuran (20.5 ml) was added 2N NaOH aq. (19.1 ml) and refluxed for 17 hours. The reaction mixture was adjusted to pH 1-2 with 1N HCl and the resulting precipitate was collected by filtration to give 4-[2-(4-butyloxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid (1.544 g).

The following compound was obtained in a manner similar to that of Preparation 25.

Preparation 26

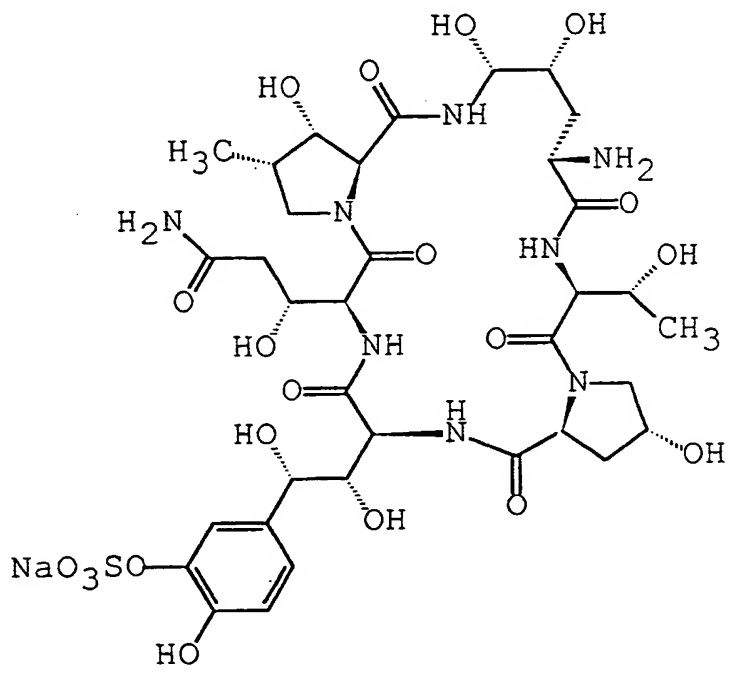
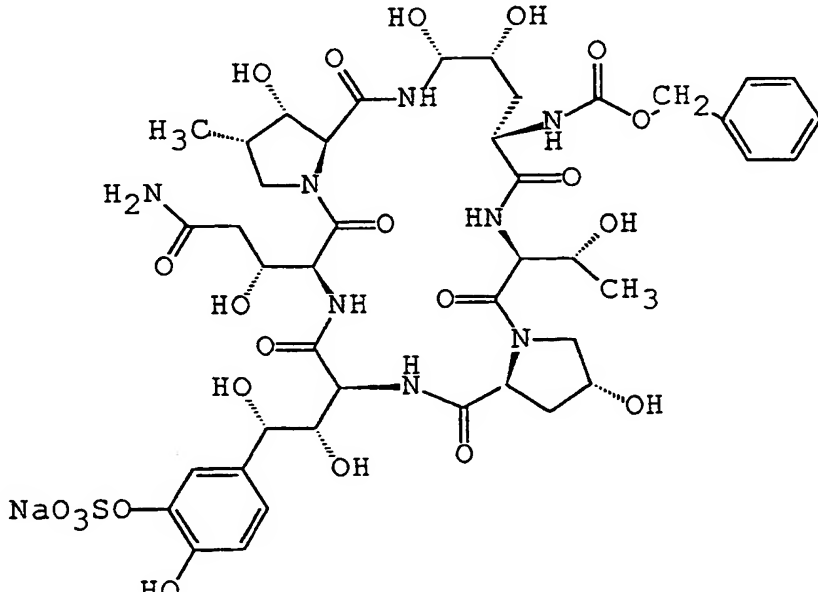
4-[2-(3-Amyloxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid

IR (KBr) : 2935.1, 2867.6, 1685.5, 1608.3, 1484.9,  
1288.2  $\text{cm}^{-1}$

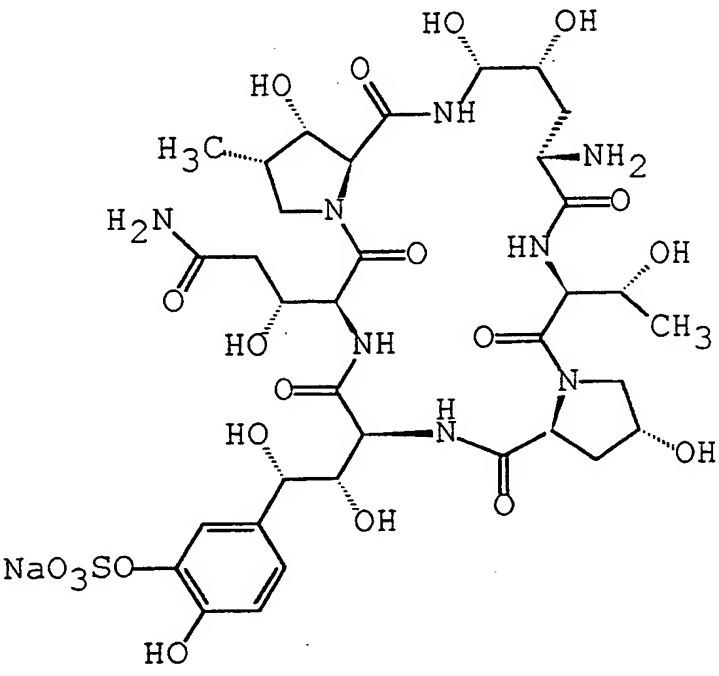
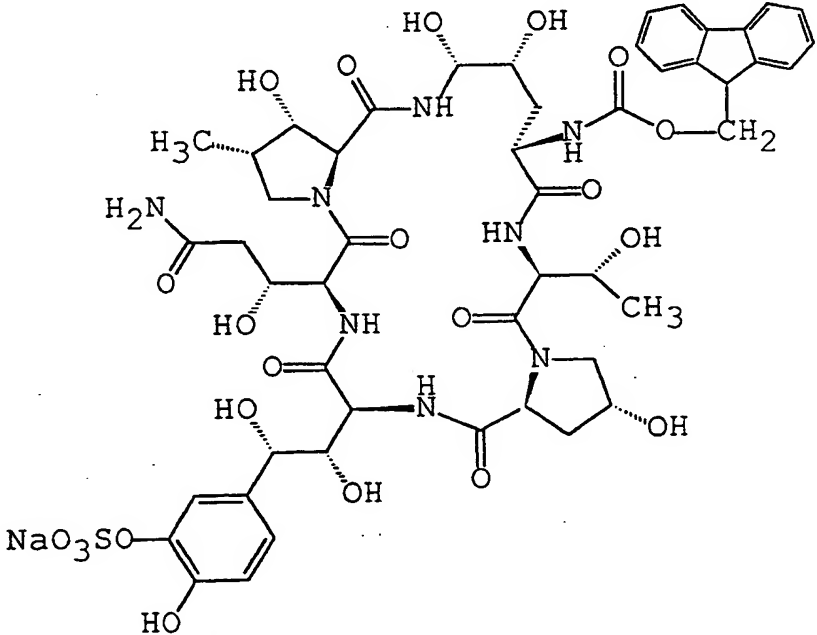
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=7.0\text{Hz}$ ), 1.39 (4H, m),  
1.75 (2H, m), 4.07 (2H, t,  $J=6.5\text{Hz}$ ), 7.19 (1H, m),  
5 7.42-7.49 (3H, m), 8.00 (4H, s), 8.89 (1H, s)

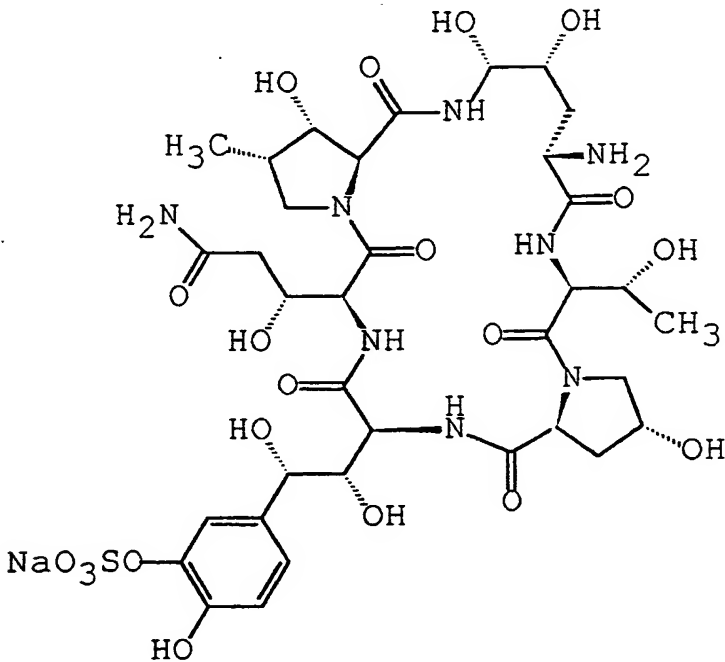
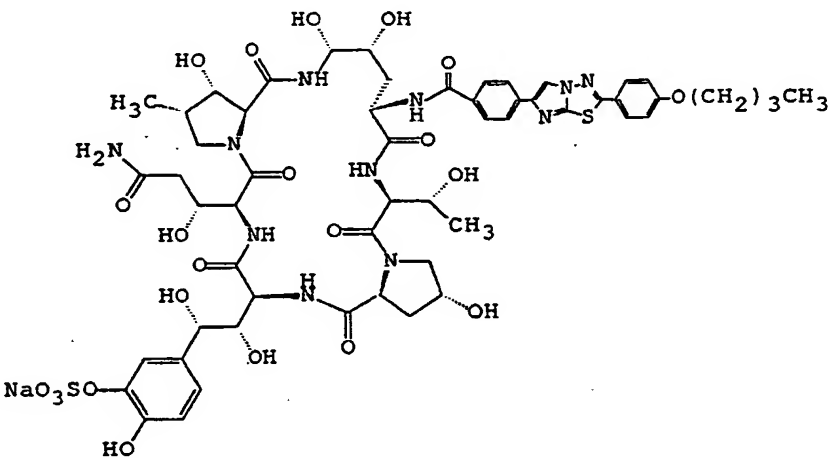
MASS (m/z) : 408 (M+1)

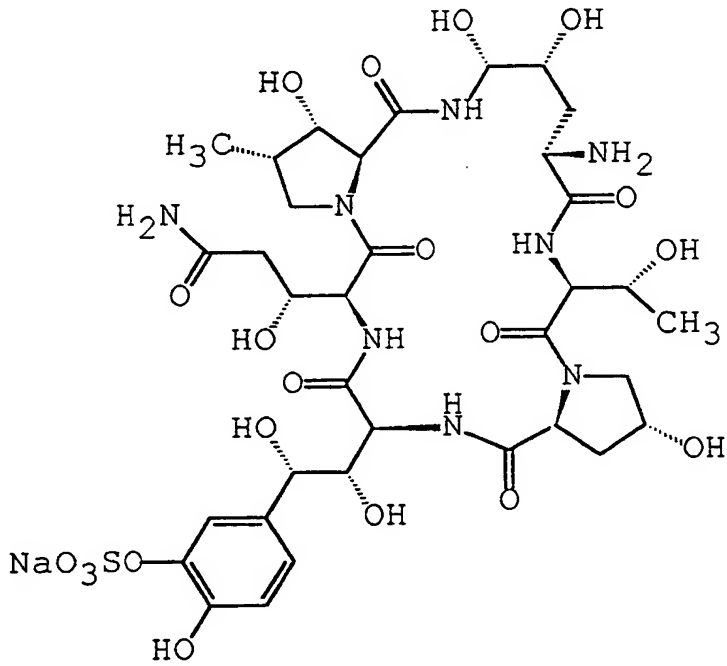
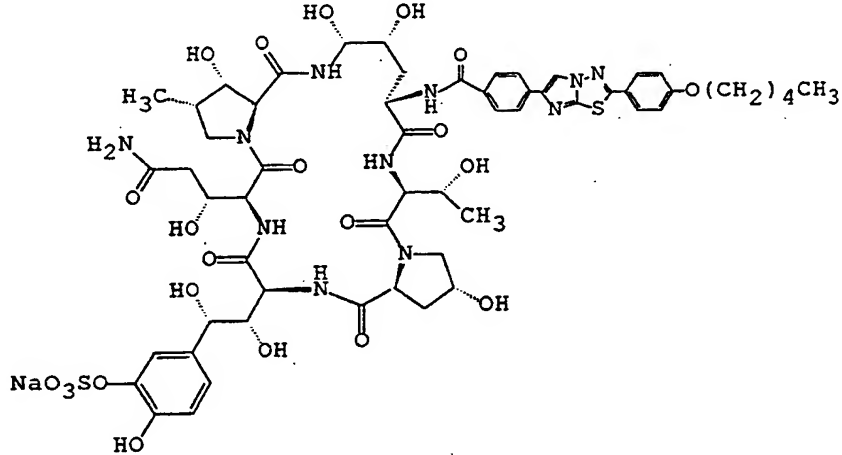
The Starting Compound used and the Object Compounds (27)  
to (30) obtained in the following Preparations 27 to 30 are  
10 given in the table as below, in which the formula of the starting  
compound is in the upper column and the formula of the object  
compounds (27) to (30) are in the lower column, respectively.

Preparation No.	Formula
	 <p>The structure is a complex molecule featuring a central chain with multiple amide and ester linkages. It includes a sodium sulfonate group (NaO<sub>3</sub>SO-) attached to a phenyl ring, which is further substituted with a hydroxyl group. The molecule also contains several hydroxyl groups and a methyl group.</p>
27	 <p>This structure is similar to the one above, but it features a different side chain. Instead of a sodium sulfonate group, it has a benzyl ester group (CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) attached to the central chain. The rest of the molecule, including the amide and ester linkages, hydroxyl groups, and methyl group, remains the same.</p>



Preparation No.	Formula
	 <p>The structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and several hydroxyl groups. The molecule is highly branched and contains a variety of functional groups.</p>
28	 <p>This structure is similar to the one above, but it features a different side chain on the right-hand side, which includes a benzyl group and a different ester linkage. The rest of the molecule, including the sodium sulfonate group and the central amide/ester core, remains the same.</p>

Preparation No.	Formula
29	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>This chemical structure is similar to the one in the previous row, but it features a different side chain. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The side chain is more complex, containing a thiazine ring system and a long alkyl chain (<math>\text{O}(\text{CH}_2)_3\text{CH}_3</math>).</p>

Preparation No..	Formula
30	
	

Preparation 27

To a solution of Starting Compound (1 g) in tetrahydrofuran (10 ml) and pH 6.86 standard buffer solution (prepared by Nacalai Tesque, Inc.) (10 ml) was added dropwise  
5 with stirring to benzyloxycarbonyl chloride (0.15 ml) in an ice-bath. The solution was then stirred for 2 hours. The reaction mixture was acidified with dilute hydrogen chloride, and evaporated under reduced pressure. The residue was  
10 dissolved in water, and subjected to column chromatography on ion exchange resin (DOWEX-50WX4 (Trademark: prepared by Dow Chemical)) eluting with water. The fractions containing the object compound were combined, and subjected to column chromatography on ODS (YMC-gel ODS-AM-S-50 (Trademark:  
15 prepared by Yamamura Chemical Lab.)) eluting with 5% acetonitrile aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give Object Compound (27) (0.78 g).

IR (KBr) : 3462, 3336, 1668, 1539, 1265  $\text{cm}^{-1}$   
20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.05 (3H, d,  $J=5.8\text{Hz}$ ), 1.78-5.53 (35H, m), 6.71-8.84 (16H, m)  
MASS (m/z) : 1068.90 ( $\text{M}-\text{Na}^+$ )

Preparation 28

To a solution of Starting Compound (54.4 g) and  
25 ethyldiisopropylamine (35 ml) in N,N-dimethylformamide (230 ml) was added 9-fluorenylmethyl chloroformate (15.8 g) at room temperature. The solution was stirred for 5 hours at the same temperature. Ethyl acetate (1.5 L) was added to the reaction mixture and the mixture was stirred for 30 minutes. The powder  
30 was collected by filtration to give crude material (94.3 g). The crude material was purified by column chromatography on DOWEX and on ODS to give Object Compound (28) (52.6 g).

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.8\text{Hz}$ ),  
1.03 (3H, d,  $J=5.6\text{Hz}$ ), 1.60-2.00 (3H, m),  
35 2.05-2.49 (4H, m), 3.18 (1H, t,  $J=11.1\text{Hz}$ ),

3.60-4.48 (17H, m), 4.68-5.36 (10H, m), 5.35 (1H, d, J=5.9Hz), 6.73 (1H, d, J=8.2Hz), 6.82 (1H, dd, J=8.2 and 1.6Hz), 6.84 (1H, m), 6.97 (1H, m), 7.04 (1H, d, J=1.6Hz), 7.27-7.46 (6H, m), 7.74-7.78 (3H, m), 7.89 (2H, d, J=7.2Hz), 8.06 (2H, t, J=7.2Hz), 8.77 (1H, s)

#### Preparation 29

To a solution of 1-hydroxybenzotriazole (216 mg) and 4-[2-(4-butyloxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid (420 mg) in N,N-dimethylformamide (20 ml) was added 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (245 mg) and the mixture was stirred for 2 hours at ambient temperature. Then to the reaction mixture was added Starting Compound (1 g) and diisopropylethylamine (0.279 ml) and the mixture was stirred for 5 hours at ambient temperature. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration and dried over under reduced pressure. The powder was added to water and subjected to ion-exchange column chromatography on DOWEX-50WX4 and eluted with water. The fractions containing the Object Compound were combined and subjected to column chromatography on ODS (YMC-gel ODS-AM S-50) and eluted with 25-30% acetonitrile aq. The fractions containing the Object Compound were combined and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give Object Compound (29) (891 mg).

NMR (DMSO-d<sub>6</sub>, δ) : 0.94 (3H, t, J=7.2Hz), 0.96 (3H, d, J=7.1Hz), 1.11 (3H, d, J=5.5Hz), 1.3-1.6 (2H, m), 1.6-2.1 (5H, m), 2.1-2.7 (4H, m), 3.25 (1H, m), 3.6-4.5 (16H, m), 4.7-5.3 (10H, m), 5.53 (1H, d, J=5.8Hz), 6.73 (1H, d, J=8.2Hz), 6.82 (1H, d, J=8.2Hz), 6.86 (1H, s), 7.05 (1H, s), 7.14 (2H, d, J=8.9Hz), 7.2-7.5 (3H, m), 7.90 (2H, d, J=8.9Hz), 7.9-8.0 (4H, m), 8.10 (1H, d, J=7.7Hz), 8.30 (1H, d, J=6.8Hz), 8.70 (1H, d, J=6.8Hz), 8.86 (1H, s)

MASS (m/z) : 1356 (M+Na<sup>+</sup>)

The following compound was obtained in a manner similar to that of Preparation 29.

Preparation 30

5 IR (KBr) : 3359, 1673.9, 1648.8, 1257.4 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=7.1Hz),

0.96 (3H, d, J=6.7Hz), 1.09 (3H, d, J=5.9Hz),

1.3-1.5 (4H, m), 1.6-2.7 (9H, m), 3.19 (1H, m),

3.6-4.6 (15H, m), 4.7-5.3 (11H, m), 5.53 (1H, d,

10 J=5.9Hz), 6.73 (1H, d, J=8.3Hz), 6.83 (1H, d,

J=8.3Hz), 6.88 (1H, s), 7.06 (1H, s), 7.14 (2H, d,

J=8.9Hz), 7.2-7.4 (3H, m), 7.90 (2H, d, J=8.9Hz),

7.97 (4H, m), 8.08 (1H, d, J=6Hz), 8.31 (1H, d, J=5Hz),

8.76 (1H, d, J=5Hz), 8.85 (1H, s), 8.86 (1H, s)

15 MASS (m/z) : 1325 (M+Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>57</sub>H<sub>70</sub>N<sub>11</sub>O<sub>22</sub>S<sub>2</sub>Na·8H<sub>2</sub>O :

C 45.87, H 5.81, N 10.32

Found : C 46.04, H 5.77, N 10.28

Preparation 31

20 A solution of 4-(4'-hydroxyphenyl)benzoic acid (25.6 g) in 10% hydrochloric acid-methanol was stirred for 3 days at room temperature. Then the solvent was evaporated in vacuo and the residue was triturated with toluene-ethyl acetate (20:1) to afford methyl 4-(4'-hydroxyphenyl)benzoate (26.5 g).

25 NMR (CDCl<sub>3</sub>, δ) : 3.94 (3H, s), 6.93 (2H, d, J=8.4Hz),

7.27 (1H, s), 7.53 (2H, d, J=8.6Hz), 7.60 (2H, d,

J=8.4Hz), 8.08 (2H, d, J=8.4Hz)

MASS (m/z) : 229 (M<sup>+</sup>+1)

30 Preparation 32

A solution of 4-(4'-hydroxyphenyl)benzoic acid (4.98 g), methyl iodide (5 ml), and sodium carbonate (7.19 g) in N,N-dimethylformamide (50 ml) was stirred for 17 hours at room temperature. The reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was extracted with

ethyl acetate. The combined organic layer was washed with water and brine. After dried over magnesium sulfate, the solution was evaporated in vacuo. The residue was triturated with n-hexane to afford methyl 4-(4'-methoxyphenyl)benzoate (5.45 g).

IR (KBr) : 1718  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.86 (3H, s), 3.93 (3H, s), 7.00 (2H, d,  $J=8.8\text{Hz}$ ), 7.57 (2H, d,  $J=8.8\text{Hz}$ ), 7.61 (2H, d,  $J=8.6\text{Hz}$ ), 8.07 (2H, d,  $J=8.6\text{Hz}$ )

10 MASS (m/z) : 243 ( $M^+ + 1$ )

#### Preparation 33

A mixture of methyl 4-[5-[4'-[4''-[3-(piperizin-1-yl)-propyloxy]phenyl]phenyl]-1,3,4-oxadiazol-2-yl]benzoate (1.13 g), 1N sodium hydroxide aqueous solution (3.5 ml), methanol (5 ml) and tetrahydrofuran (5 ml) was refluxed for 17 hours. The mixture was cooled down to room temperature and evaporated in vacuo. To the residue was added 1N hydrochloric acid aqueous solution. The powder was obtained by filtration to give 4-[5-[4'-[4''-[3-(piperizin-1-yl)-propyloxy]phenyl]phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid hydrochloric acid salt (1.01 g).

IR (KBr) : 3431, 2943, 2877, 2694, 2640, 2571, 2543, 1699  $\text{cm}^{-1}$

25 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.56 (2H, m), 1.78 (4H, m), 2.19 (2H, m), 3.17 (6H, m), 4.14 (2H, t,  $J=7.0\text{Hz}$ ), 7.09 (2H, d,  $J=8.8\text{Hz}$ ), 7.77 (2H, d,  $J=8.8\text{Hz}$ ), 7.92 (2H, d,  $J=8.6\text{Hz}$ ), 8.17 (2H, d,  $J=8.6\text{Hz}$ ), 8.20 (2H, d,  $J=8.5\text{Hz}$ ), 8.27 (2H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 484 ( $M^+ + 1$ ) free

#### Preparation 34

35 A solution of methyl pyrazole-4-carboxylate (10 g) in N,N-dimethylformamide (100 ml) was treated with potassium carbonate (10.95 g) and 1-bromodecane (19.31 g) and the mixture was stirred for 16 hours at room temperature. Ethyl acetate was added and the solution was washed with water (6x), dried

over magnesium sulfate and the evaporated residue was purified by silica gel chromatography (5:1 hexane-ethyl acetate elution) to give methyl 1-decylpyrazole-4-carboxylate (19.4 g) as a white solid.

5        NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.84-0.90 (3H, m), 1.25 (14H, br s),  
         1.83-1.90 (2H, m), 3.82 (3H, s), 4.15 (2H, t, J=7Hz),  
         7.87 (1H, s), 7.90 (1H, s)

         MASS (m/z) : 267 (M<sup>+</sup>)

#### Preparation 35

10        A solution of methyl 4-(4'-hydroxyphenyl)benzoate (2 g)  
         in N,N-dimethylformamide (20 ml) was treated with potassium  
         carbonate (1.21 g) and 3-phenoxypropylbromide (2.07 g) was  
         stirred for 15 hours at room temperature and 4 hours at 85°C.  
         After cooling, the reaction was quenched with water and the  
15        precipitate was collected, washed thoroughly with water and  
         dried to give methyl 4-[4'-(3-phenoxypropyloxy)phenyl]-  
         benzoate (2.6 g).

         NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 2.14-2.26 (2H, m), 3.87 (3H, s),  
         4.12-4.29 (4H, m), 6.89-6.98 (3H, m), 7.08 (2H, d,  
20        J=8.8Hz), 7.25-7.33 (2H, m), 7.70 (2H, d, J=8.8Hz),  
         7.78 (2H, d, J=8.5Hz), 8.00 (2H, d, J=8.4Hz)

         MASS (m/z) : 363 (M<sup>+</sup>)

#### Preparation 36

25        A solution of methyl 4-(4'-hydroxyphenyl)benzoate (5 g)  
         in N,N-dimethylformamide (50 ml) was treated with potassium  
         carbonate (6.06 g) and allyl bromide (2.46 ml), then heated  
         at 60°C for 3 hours. After cooling, the reaction mixture was  
         poured into ice-water (~200 ml) and the resulting precipitate  
         was collected by filtration, washed with water, then isopropyl  
30        ether, then dried to give methyl 4-[4'-  
         (allyloxy)phenyl]benzoate (5.55 g) as a solid.

         mp : 148-149°C

         NMR (CDCl<sub>3</sub>,  $\delta$ ) : 3.93 (3H, s), 4.29-4.61 (2H, m), 5.28-  
         5.49 (2H, m), 5.99-6.18 (1H, m), 7.00 (2H, d,  
35        J=8.8Hz), 7.56 (2H, d, J=8.8Hz), 7.61 (2H, d,



J=8.5Hz), 8.07 (2H, d, J=8.5Hz)

MASS (m/z) : 269 (M<sup>+</sup>)

#### Preparation 37

A solution of 4-(4'-hydroxyphenyl)benzoic acid (4 g) and  
5 1N sodium hydroxide (41 ml) in dimethyl sulfoxide (40 ml) was  
heated for 30 minutes at 85°C, then treated with  
4-phenoxybutyl bromide (6.42 g) and heating continued for 8  
hours. After cooling, the reaction was poured into water and  
adjusted to pH 2 and the resulting precipitate was collected,  
10 washed with water, and dried to give 4-[4'-(4-  
phenoxybutyloxy)phenyl]benzoic acid (6.7 g).

IR (KBr) : 1683.6, 1594.8, 1535.1 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.89 (4H, br s), 3.34 (1H, br s),  
4.04-4.10 (4H, m), 6.91-6.95 (3H, m), 7.05 (2H, d,  
15 J=7.9Hz), 7.24-7.30 (2H, m), 7.66-7.76 (4H, m), 7.98  
(2H, d, J=7.8Hz)

#### Preparation 38

A mixture of 4-[4'-(4-phenoxybutyloxy)phenyl]benzoic  
acid (5 g), 1-hydroxybenzotriazole (2.24 g) and 1-ethyl-3-  
20 (3'-dimethylaminopropyl)carbodiimide hydrochloride (3.97 g)  
in N,N-dimethylformamide (70 ml) was stirred for 18 hours at  
room temperature, then treated with tert-butylcarbazate (2.19  
g) and the mixture was stirred for further 4 hours at ambient  
temperature. Water was added and the precipitate was  
25 collected, washed with water, and dried to give N-(tert-  
butoxycarbonyl)-N'-[4-[4'-(4-  
phenoxybutyloxy)phenyl]benzoyl]hydrazine (6 g) as a solid.

IR (KBr) : 1650.8, 1492.6, 1290.1, 1249.6 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.44 (9H, br s), 1.90 (4H, br s),  
30 4.04-4.10 (4H, m), 6.88-6.96 (3H, m), 7.05 (2H, d,  
J=8.7Hz), 7.24-7.32 (2H, m), 7.69 (2H, d, J=8.8Hz),  
7.75 (2H, d, J=8.5Hz), 7.92 (2H, d, J=8.2Hz), 8.91  
(1H, s), 10.21 (1H, s)

#### Preparation 39

35 A solution of N-(tert-butoxycarbonyl)-N'-[4-[4'-(4-

phenoxybutyloxy)phenyl]benzoyl]hydrazine (6 g) in trifluoroacetic acid (40 ml) was stirred for 2 hours at room temperature, then evaporated under reduced pressure, dissolved in water, then adjusted to pH 8 with saturated sodium hydrogen carbonate solution. The precipitate was collected, washed with water, and dried to give 4-[4'-(4-phenoxybutyloxy)phenyl]benzoylhydrazine (5 g).

IR (KBr) : 3282.3, 1604.5  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.89 (4H, br s), 4.04-4.09 (4H, m), 4.55 (2H, br), 6.83-6.96 (3H, m), 7.04 (2H, d,  $J=8.6\text{Hz}$ ), 7.24-7.28 (2H, m), 7.64-7.72 (4H, m), 7.88 (2H, d,  $J=8.3\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 377 ( $\text{M}^+$ )

#### Preparation 40

A solution of 4-methoxycarbonylbenzoylhydrazine (432 mg) in tetrahydrofuran (15 ml)-pyridine (5 ml) was treated with 4-[4'-(8-methoxy-n-octyloxy)phenyl]benzoic acid benzotriazol-1-yl ester (1.054 g) and the mixture was stirred for 72 hours at room temperature, then water (~100 ml) was added to the reaction mixture and the precipitate was collected, washed with water and dried to give N-[4-[4'-(8-methoxy-n-octyloxy)phenyl]benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine (1.10 g).

IR (KBr) : 3220.5, 2933.2, 2856.1, 1724.0, 1679.7, 1654.6  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.20-1.60 (10H, m), 1.60-1.80 (2H, m), 3.21 (3H, s), 3.21-3.33 (2H, m), 3.90 (3H, s), 4.02 (2H, t,  $J=6.9\text{Hz}$ ), 7.05 (2H, d,  $J=8.7\text{Hz}$ ), 7.70 (2H, d,  $J=8.6\text{Hz}$ ), 7.79 (2H, d,  $J=8.3\text{Hz}$ ), 7.99 (2H, d,  $J=8.3\text{Hz}$ ), 8.04 (2H, d,  $J=8.5\text{Hz}$ ), 8.11 (2H, d,  $J=8.5\text{Hz}$ ), 10.60 (1H, s), 10.70 (1H, s)

MASS (m/z) : 533 ( $\text{M}^+$ )

#### Preparation 41

A suspension of N-(4-methoxybenzoyl)-N'-(4-methoxycarbonylbenzoyl)hydrazine (10 g) and di-phosphorus

pentasulfide (6.77 g) in tetrahydrofuran (100 ml) was refluxed for 3 hours. The reaction mixture was cooled, poured into water (300 ml), stirred for 30 minutes and extracted with dichloromethane (1500 ml) and methanol (300 ml). The organic layer was washed with water and brine, dried over magnesium sulfate and evaporated under reduced pressure. The residue was triturated with acetonitrile. The solid was collected by filtration and dried under reduced pressure to give methyl 4-[5-(4-methoxyphenyl)-1,3,4-thiadiazo

5  
10

IR (KBr) : 2952.5, 2840.6, 1714.4, 1606.4, 1278.6,  
1251.6  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.89 (3H, s), 3.96 (3H, s), 7.01 (2H, d,  $J=8.9\text{Hz}$ ), 7.97 (2H, d,  $J=8.9\text{Hz}$ ), 8.07 (2H, d,  $J=8.7\text{Hz}$ ), 8.16 (2H, d,  $J=8.7\text{Hz}$ )

15

MASS ( $m/z$ ) : 327 ( $M^++1$ )

#### Preparation 42

To a solution of borontribromide (2.0M in dichloromethane, 103 ml) was added dropwise methyl 4-[5-(4-methoxyphenyl)-1,3,4-thiadiazo

20

The reaction mixture was allowed to warm to room temperature, and the mixture was stirred overnight. The reaction mixture was poured into ice-water (1000 ml). The precipitate was collected by filtration, washed with water and dried under reduced pressure at 60°C to give a mixture of methyl 4-[5-(4-hydroxyphenyl)-1,3,4-thiadiazo

25

4-[5-(4-hydroxyphenyl)-1,3,4-thiadiazo

#### Preparation 43

To a suspension of a mixture of methyl 4-[5-(4-hydroxyphenyl)-1,3,4-thiadiazo

30

hydroxyphenyl)-1,3,4-thiadiazo

potassium carbonate (531 mg) and N,N-dimethylformamide (3 ml) was added 4-phenoxybutylbromide (880 mg) and the mixture was stirred at 100°C (bath temperature) for 2 hours. After cooling,

35

the mixture was added to 0.1N hydrochloric acid (100 ml). The resulting precipitate was collected by filtration and washed with water. To this material was added tetrahydrofuran (20 ml), ethanol (20 ml) and 10% sodium hydroxide aqueous solution (1.39 ml). The mixture was refluxed for 2 hours. After cooling, the reaction mixture was diluted with water (100 ml), adjusted to pH 1.8 with 1N hydrochloric acid, then extracted with a mixture of dichloromethane (1000 ml), tetrahydrofuran (200 ml) and methanol (200 ml). The organic layer was washed with brine and dried over magnesium sulfate. The solvents were removed under reduced pressure and the residue was triturated with acetonitrile. The solid was collected by filtration and dried to give 4-[5-[4-(4-phenoxybutyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid (685 mg).

IR (KBr) : 3371.0, 2674.8, 2547.5, 1685.5, 1604.5, 1249.6  $\text{cm}^{-1}$

#### Preparation 44

To a suspension of a mixture of methyl 4-[5-(4-hydroxyphenyl)-1,3,4-thiadiazol-2-yl]benzoate and 4-[5-(4-hydroxyphenyl)-1,3,4-thiadiazol-2-yl]benzoic acid (2.0 g), potassium carbonate (14.6 g) and N,N-dimethylformamide (15 ml) was added 1,5-dibromopentane (10 ml) and the mixture was stirred at 100°C (bath temperature) for 1.5 hours. The resulting mixture was neutralized by 0.1N hydrochloric acid and extracted with dichloromethane. The organic layer was washed with brine and dried over magnesium sulfate. The solvents were removed under reduced pressure and the residue was triturated with n-hexane. The solid was collected by filtration and dried. To this compound was added phenol (1.43 g), potassium carbonate (2.10 g) and N,N-dimethylformamide (30 ml), and the mixture was stirred at 100°C (bath temperature) for 20 hours. After cooling, the reaction mixture was poured into saturated sodium hydrogen carbonate aqueous solution. The resulting precipitate was collected by filtration, washed with water. To this compound was added tetrahydrofuran (20

ml), ethanol (20 ml) and 10% sodium hydroxide aqueous solution (2.6 ml). The mixture was refluxed for 1.5 hours. The reaction mixture was diluted with water, acidified with 1N hydrochloric acid (10 ml). The resulting precipitate was collected by filtration, washed with water, dried under reduced pressure to give 4-[5-[4-(5-phenoxy-n-pentyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid (2.47 g), that was used crude in the next reaction.

MASS (m/z) : 461 ( $M^+ + 1$ )

10 Preparation 45

To a suspension of a mixture of methyl 4-[5-(4-hydroxyphenyl)-1,3,4-thiadiazol-2-yl]benzoate and 4-[5-(4-hydroxyphenyl)-1,3,4-thiadiazol-2-yl]benzoic acid (3.12 g), potassium carbonate (22.07 g) and N,N-dimethylformamide (15 ml) was added 1,5-dibromopentane (15 ml) and the mixture was stirred at 100°C (bath temperature) for 5 hours. The resulting mixture was neutralized by 0.1N hydrochloric acid and extracted with dichloromethane. The organic layer was washed with brine and dried over magnesium sulfate. The solvents were removed under reduced pressure and the residue was triturated with n-hexane. The solid was collected by filtration and dried to give a crude powder (3.71 g). To the crude powder (2.11 g) was added methanol (10 ml) and sodium methoxide (28% in methanol) (10 ml), and refluxed for 2 hours. Then to the reaction mixture was added sodium methoxide (28% in methanol) (5 ml) and refluxed for 1.5 hours. After cooling, the reaction mixture was added to water and tetrahydrofuran, stirred overnight and adjusted to pH 2 with 4N hydrochloric acid. The resulting precipitate was collected by filtration, washed with acetonitrile and dried under reduced pressure to give 4-[5-[4-(5-methoxy-n-pentyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid (1.34 g).

IR (KBr) : 2940.9, 2865.7, 2663.2, 2549.4, 1685.5,  
1604.5, 1432.9, 1413.6, 1292.1,  
1253.5  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.3-1.7 (4H, m), 1.7-2.0 (2H, m),  
3.23 (3H, s), 3.36 (2H, m), 4.07 (2H, t,  $J=6.4\text{Hz}$ ),  
7.13 (2H, d,  $J=8.8\text{Hz}$ ), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 8.12  
(4H, s)

5        MASS (m/z) : 399 ( $M^++1$ )

Preparation 46

To a solution of piperidine (2.98 g) and methyl 6-chloronicotinate (5.00 g) in *N,N*-dimethylformamide (75 ml) was added potassium carbonate (12.08 g). The mixture was stirred  
10 at 100°C for 3 hours. After cooling to ambient temperature, to the reaction mixture was added water (100 ml) and then the mixture was stirred for 15 minutes at ambient temperature. The resulting precipitates were filtered, washed with water, and dried to give methyl 6-(1-piperidyl)nicotinate (5.55 g), as  
15 a white solid.

IR (KBr) : 2941, 2850, 1701, 1608, 1552, 1508, 1435,  
1415  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.5-1.8 (6H, m), 3.6-3.7 (4H, m),  
3.86 (3H, s), 6.57 (1H, d,  $J=9.1\text{Hz}$ ), 7.98 (1H, dd,  
20  $J=9.1$  and  $2.4\text{Hz}$ ), 8.78 (1H, d,  $J=2.0\text{Hz}$ )

MASS (m/z) : 221 ( $M^++1$ )

Preparation 47

To a solution of methyl 6-(1-piperidyl)nicotinate (5.00 g) in a mixed solvent of ethanol (25 ml) and tetrahydrofuran  
25 (10 ml) was added hydrazine monohydrate (11.0 ml). The solution was refluxed for 6 hours, during which period additional hydrazine monohydrate (11.0 ml) was added to the mixture. After cooling to ambient temperature, the reaction mixture was added to water (100 ml) and then stirred for 20  
30 minutes at ambient temperature. The resulting precipitates were filtered, washed with water, and dried to give 6-(1-piperidyl)nicotinoylhydrazine (3.44 g), as a white solid.

IR (KBr) : 3300, 2931, 2846, 1649, 1608, 1554, 1502,  
1417, 1348, 1242  $\text{cm}^{-1}$

35        NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.5-1.8 (6H, m), 3.4-3.8 (6H, m), 6.61

(1H, d, J=8.9Hz), 7.51 (1H, br s), 7.85 (1H, dd, J=9.0 and 2.5Hz), 8.54 (1H, d, J=2.0Hz)

MASS (m/z) : 221 ( $M^+ + 1$ )

#### Preparation 48

5 To a solution of N-[6-(1-piperidyl)nicotinoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine (2.00 g) in pyridine (40 ml) was added phosphorus pentasulfide (1.74 g). The mixture was refluxed for 4 hours. After cooling to ambient temperature, the reaction mixture was poured into cold water (150 ml) and  
10 the mixture was adjusted to pH 11 with 1N sodium hydroxide aqueous solution and the mixture was stirred for 30 minutes at ambient temperature. The resulting precipitates were filtered, washed with water and dried to give methyl 4-[5-[6-(1-piperidyl)pyridin-3-yl]-1,3,4-thiadiazol-2-  
15 yl]benzoate (1.59 g), as a yellow solid.

IR (KBr) : 2933, 2848, 1720, 1604, 1433, 1279,

1109  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.6-1.8 (6H, m), 3.6-3.8 (4H, m), 3.96  
(3H, s), 6.73 (1H, d, J=9.1Hz), 8.06 (2H, d, J=8.7Hz),  
20 8.14 (1H, dd, J=9.2 and 2.9Hz), 8.16 (2H, d, J=8.6Hz),  
8.70 (1H, d, J=2.2Hz)

MASS (m/z) : 381 ( $M^+ + 1$ )

#### Preparation 49

To a refluxing suspension of methyl 4-[5-[2-(1-  
25 piperidyl)pyridin-5-yl]-1,3,4-thiadiazol-2-yl]benzoate (1.50 g) in a mixed solvent of tetrahydrofuran (75 ml) and ethanol (15 ml) was added dropwise 10% sodium hydroxide aqueous solution (3.15 ml). The mixture was refluxed for 1.5 hours and cooled to ambient temperature. To the reaction mixture  
30 was added water (100 ml) and the pH was adjusted to 1 with 1N hydrochloric acid (15 ml). The mixture was stirred for 30 minutes at ambient temperature and the resulting precipitates were filtered, washed with water and dried to give 4-[5-[6-(1-piperidyl)pyridin-3-yl]-1,3,4-thiadiazol-2-  
35 yl]benzoic acid hydrochloride (1.36 g), as a yellow solid.

IR (KBr) : 3479, 2935, 2854, 1695, 1605, 1431, 1281,  
1250  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.5-1.7 (6H, m), 3.6-3.7 (4H, m),  
6.99 (1H, d,  $J=9.1\text{Hz}$ ), 8.08 (1H, dd,  $J=9.1$  and  $2.5\text{Hz}$ ),  
8.11 (4H, s), 8.71 (1H, d,  $J=2.4\text{Hz}$ )

MASS (m/z) : 367 ( $M^++1$ ) (free)

#### Preparation 50

To a suspension of 4-[5-[6-(1-piperidyl)pyridin-3-yl]-  
1,3,4-thiadiazol-2-yl]benzoic acid hydrochloride (1.20 g) in  
methylen chloride (60 ml) was added triethylamine (0.57 ml)  
and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide  
hydrochloride (1.43 g). The mixture was stirred for 6 hours  
at ambient temperature. To the reaction mixture was added  
water and the organic layer was separated, washed with aqueous  
sodium hydrogen carbonate solution and saturated sodium  
chloride solution, and dried over magnesium sulfate, and  
concentrated in vacuo. Diisopropyl ether was added to the  
residue and the precipitates were filtered, washed with the  
same solvent, and dried to give 4-[5-[6-(1-  
piperidyl)pyridin-3-yl]-1,3,4-thiadiazol-2-yl]benzoic acid  
benzotriazol-1-yl ester (1.18 g), as a yellow solid.

IR (KBr) : 2931, 2854, 1778, 1600, 1547, 1512, 1431,  
1358, 1242, 993  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.6-1.8 (6H, m), 3.6-3.8 (4H, m), 6.75  
(1H, d,  $J=9.1\text{Hz}$ ), 7.4-7.7 (3H, m), 8.13 (1H, d,  
 $J=8.2\text{Hz}$ ), 8.16 (1H, dd,  $J=9.1$  and  $2.5\text{Hz}$ ), 8.24 (2H,  
d,  $J=8.6\text{Hz}$ ), 8.40 (2H, d,  $J=8.6\text{Hz}$ ), 8.72 (1H, d,  
 $J=2.3\text{Hz}$ )

MASS (m/z) : 484 ( $M^++1$ )

#### Preparation 51

A solution of methyl 4-(4'-hydroxyphenyl)benzoate (2.02  
g), n-butylbromide (3 ml) and sodium carbonate (3.6 g) in  
N,N-dimethylformamide was stirred for 17 hours at  $80^\circ\text{C}$ . The  
reaction mixture was cooled to room temperature and  
partitioned between ethyl acetate and water. The aqueous



layer was extracted with ethyl acetate. The combined organic layer was washed with water and brine. After dried over magnesium sulfate, the solution was evaporated in vacuo. The residue was triturated with n-hexane to afford methyl 4-(4'-butyloxyphenyl)benzoate (2.45 g).

IR (KBr) : 2956, 2935, 2873, 1722  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.94 (3H, d,  $J=7.3\text{Hz}$ ), 1.45 (2H, qt,  $J=7.3$  and  $6.9\text{Hz}$ ), 1.70 (2H, tt,  $J=6.9$  and  $6.9\text{Hz}$ ), 4.03 (2H, t,  $J=6.9\text{Hz}$ ), 7.04 (2H, d,  $J=8.8\text{Hz}$ ), 7.68 (2H, d,  $J=8.8\text{Hz}$ ), 7.78 (2H, d,  $J=8.5\text{Hz}$ ), 8.00 (2H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 285 ( $\text{M}^++1$ )

The following compounds [Preparations 52 to 54] were obtained in a manner similar to that of Preparation 51.

Preparation 52

Methyl 4-(4'-n-pentyloxyphenyl)benzoate

IR (KBr) : 2958, 2935, 2866, 1722  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=7.0\text{Hz}$ ), 1.39 (4H, m), 1.74 (2H, m), 3.87 (3H, s), 4.02 (2H, t,  $J=6.4\text{Hz}$ ), 7.04 (2H, t,  $J=8.8\text{Hz}$ ), 7.69 (2H, d,  $J=8.8\text{Hz}$ ), 7.78 (2H, d,  $J=8.5\text{Hz}$ ), 8.00 (2H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 299 ( $\text{M}^++1$ )

Preparation 53

Methyl 4-(4'-n-hexyloxyphenyl)benzoate

IR (KBr) : 2954, 2933, 2866, 1724  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, m), 1.20-1.87 (8H, m), 3.87 (3H, s), 4.02 (2H, m), 7.04 (2H, d,  $J=8.7\text{Hz}$ ), 7.68 (2H, d,  $J=8.7\text{Hz}$ ), 7.78 (2H, d,  $J=8.4\text{Hz}$ ), 8.00 (2H, d,  $J=8.4\text{Hz}$ )

MASS (m/z) : 313 ( $\text{M}^++1$ )

Preparation 54

Methyl 4-(4'-n-heptyloxyphenyl)benzoate

IR (KBr) : 2956, 2931, 2856, 1724  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, m), 1.20-1.80 (10H, m), 3.87 (3H, s), 4.05 (2H, m), 7.04 (2H, d,  $J=8.7\text{Hz}$ ),

7.69 (2H, d, J=8.7Hz), 7.78 (2H, d, J=8.5Hz), 8.00  
(2H, d, J=8.5Hz)

MASS (m/z) : 327 ( $M^+$ +1)

#### Preparation 55

5 A solution of methyl 4-[4'-(3-bromopropoxy)phenyl]benzoate (1.5 g), potassium carbonate (1.2 g) and cis-2,6-dimethylmorpholine (990.6 mg) in N,N-dimethylformamide was stirred for 15 hours at room temperature, then diluted with ethyl acetate and washed with water (5x),  
10 dried over magnesium sulfate, evaporated, then purified by silica gel chromatography (20:1 dichloromethane-ethanol elution) to give methyl 4-[4'-(3-(2,6-dimethylmorpholino)propoxy]phenyl]benzoate (755 mg).

NMR ( $CDCl_3$ ,  $\delta$ ) : 1.18 (6H, d, J=6.3Hz), 1.70-1.90 (2H,  
15 m), 2.00-2.14 (2H, m), 2.50-2.65 (2H, m), 2.82 (2H, d, J=11Hz), 3.74 (2H, br s), 3.93 (3H, s), 4.08 (2H, t, J=6.2Hz), 6.98 (2H, d, J=8.7Hz), 7.56 (2H, d, J=8.7Hz), 7.61 (2H, d, J=8.3Hz), 8.08 (2H, d, J=8.3Hz)

20 MASS (m/z) : 384 ( $M^+$ )

The following compound was obtained in a manner similar to that of Preparation 55.

#### Preparation 56

25 Methyl 4-[4'-(3-(piperizin-1-yl)propyloxy)phenyl]-benzoate

IR (KBr) : 2933, 2852, 2771, 1718  $cm^{-1}$

NMR ( $CDCl_3$ ,  $\delta$ ) : 1.47 (2H, m), 1.64 (4H, m), 2.04 (2H, tt, J=6.3 and 6.3Hz), 2.51 (6H, m), 3.93 (3H, s),  
30 4.07 (2H, t, J=6.3Hz), 6.98 (2H, d, J=8.8Hz), 7.56 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.6Hz), 8.07 (2H, d, J=8.6Hz)

MASS (m/z) : 354 ( $M^+$ +1)

#### Preparation 57

35 A mixture of N-[4-(4'-allyloxyphenyl)benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine (1.5 g) and phosphorus

oxychloride (15 ml) was heated to reflux for 6 hours, then cooled to room temperature and poured into ice-water, stirred for ~2 hours then filtered. The resulting solid was washed thoroughly with water and dried at 50°C under vacuum to give  
5 methyl 4-[5-[4'-(4"-allyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoate as a solid.

IR (KBr) : 1720.2, 1650.8, 1284.4, 1255.4  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 3.98 (3H, s), 4.61 (2H, d,  $J=5.3\text{Hz}$ ),  
5.30-5.50 (2H, m), 6.03-6.17 (1H, m), 7.04 (2H, d,  
10  $J=8.8\text{Hz}$ ), 7.61 (2H, d,  $J=8.8\text{Hz}$ ), 7.74 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.20 (2H, d,  $J=8.5\text{Hz}$ ), 8.23 (4H, s)

MASS ( $m/z$ ) : 413 ( $M^+$ )

The following compounds [Preparations 58 to 68] were obtained in a manner similar to that of Preparation 57.

15 Preparation 58

Methyl 4-[5-[4'-(4"-methoxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoate

IR (KBr) : 1716  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.88 (3H, s), 3.98 (3H, s), 7.02 (2H,  
20 d,  $J=8.8\text{Hz}$ ), 7.61 (2H, d,  $J=8.8\text{Hz}$ )

MASS ( $m/z$ ) : 387 ( $M^++1$ )

Preparation 59

Methyl 4-[5-[4'-(4"-butyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoate

25 IR (KBr) : 2956, 2933, 2871, 1720  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00 (3H, t,  $J=7.3\text{Hz}$ ), 1.54 (2H, qt,  
 $J=7.3$  and  $7.0\text{Hz}$ ), 1.82 (2H, tt,  $J=7.0$  and  $7.0\text{Hz}$ ),  
3.98 (3H, s), 4.03 (2H, t,  $J=7.0\text{Hz}$ ), 7.00 (2H, d,  
 $J=8.7\text{Hz}$ ), 7.60 (2H, d,  $J=8.7\text{Hz}$ ), 7.73 (2H, d,  
30  $J=8.4\text{Hz}$ ), 8.22 (6H, m)

MASS ( $m/z$ ) : 429 ( $M^++1$ )

Preparation 60

Methyl 4-[5-[4'-(4"-n-pentyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoate

35 IR (KBr) : 2956, 2931, 2870, 1720  $\text{cm}^{-1}$

NMR (CDCl<sub>3</sub>, δ) : 0.995 (3H, t, J=7.0Hz), 1.43 (4H, m),  
1.83 (2H, tt, J=7.0Hz), 3.98 (3H, s), 4.02 (2H, t,  
J=7.0Hz), 7.00 (2H, d, J=8.7Hz), 7.60 (2H, d,  
J=8.7Hz), 7.73 (2H, d, J=8.4Hz), 8.23 (2H, m)

5        MASS (m/z) : 443 (M<sup>+</sup>+1)

Preparation 61

Methyl 4-[5-[4'-(4"-n-hexyloxyphenyl)phenyl]-1,3,4-  
oxadiazol-2-yl]benzoate

IR (KBr) : 2954, 2933, 2870, 1722 cm<sup>-1</sup>

10        NMR (CDCl<sub>3</sub>, δ) : 0.92 (3H, t, J=6.7Hz), 1.39 (6H, m),  
1.82 (2H, tt, J=6.9Hz), 3.98 (3H, s), 4.02 (2H, t,  
J=6.5Hz), 7.00 (2H, d, J=8.6Hz), 7.60 (2H, d,  
J=8.6Hz), 7.73 (2H, d, J=8.3Hz), 8.22 (6H, m)

MASS (m/z) : 457 (M<sup>+</sup>+1)

15        Preparation 62

Methyl 4-[5-[4'-(4"-n-heptyloxyphenyl)phenyl]-1,3,4-  
oxadiazol-2-yl]benzoate

IR (KBr) : 2954, 2931, 2856, 1722 cm<sup>-1</sup>

20        NMR (CDCl<sub>3</sub>, δ) : 0.90 (3H, br), 1.20-2.00 (10H, br),  
3.98 (3H, s), 4.02 (2H, br), 7.00 (2H, d, J=7.6Hz),  
7.59 (2H, d, J=7.6Hz), 7.73 (2H, d, J=6.8Hz), 8.20  
(6H, m)

MASS (m/z) : 471 (M<sup>+</sup>+1)

Preparation 63

25        Methyl 4-[5-[4'-[4"-[3-(piperizin-1-  
yl)propyloxy]phenyl]phenyl]-1,3,4-oxadiazol-2-yl]benzoate

IR (KBr) : 2931, 2852, 2804, 2769, 1720 cm<sup>-1</sup>

30        NMR (CDCl<sub>3</sub>, δ) : 1.51 (2H, m), 1.74 (4H, m), 2.14 (2H,  
m), 2.64 (6H, m), 3.98 (3H, s), 4.10 (2H, t, J=6.2Hz),  
7.00 (2H, d, J=8.8Hz), 7.60 (2H, d, J=8.7Hz), 7.73  
(2H, d, J=8.20Hz), 8.20 (2H, d, J=8.5Hz), 8.23 (4H,  
s)

MASS (m/z) : 498 (M<sup>+</sup>+1)

Preparation 64

35        Methyl 4-[5-(1-n-decylpyrazol-4-yl)-1,3,4-oxadiazol-

2-yl]benzoate

NMR (CDCl<sub>3</sub>, δ) : 0.84-0.91 (3H, m), 1.26-1.32 (14H, m),  
1.80-2.00 (2H, m), 3.97 (3H, s), 4.21 (2H, t,  
J=7.1Hz), 7.26 (1H, s), 8.09 (1H, s), 8.26 (4H, s)

5 MASS (m/z) : 411 (M<sup>+</sup>)

Preparation 65

Methyl 4-[5-[4'-[4''-(3-phenoxypropyloxy)-  
phenyl]phenyl]-1,3,4-oxadiazol-2-yl]benzoate

IR (KBr) : 1718.3, 1600.6, 1490.7, 1280.5,

10 1245.8 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 2.26-2.35 (2H, m), 3.98 (3H, s),  
4.16-4.27 (4H, m), 6.91-7.05 (5H, m), 7.26-7.33 (2H,  
m), 7.60 (2H, d, J=8.7Hz), 7.73 (2H, d, J=8.4Hz),  
8.20 (2H, d, J=8.4Hz), 8.23 (4H, s)

15 MASS (m/z) : 507 (M<sup>+</sup>)

Preparation 66

Methyl 4-[5-[4'-[4''-(4-phenoxybutyloxy)-  
phenyl]phenyl]-1,3,4-oxadiazol-2-yl]benzoate

IR (KBr) : 1720.2, 1602.6 cm<sup>-1</sup>

20 NMR (CDCl<sub>3</sub>, δ) : 2.02 (4H, br s), 3.93 (3H, s), 3.97-  
4.06 (4H, m), 6.83-7.04 (6H, m), 7.26-7.33 (1H, m),  
7.60 (2H, d, J=8.7Hz), 7.89 (2H, d, J=8.7Hz),  
8.18-8.23 (6H, m)

MASS (m/z) : 521 (M<sup>+</sup>)

25 Preparation 67

Methyl 4-[5-[4'-[4''-(8-methoxy-n-octyloxy)phenyl]-  
phenyl]-1,3,4-oxadiazol-2-yl]benzoate

IR (KBr) : 1720.2 cm<sup>-1</sup>

30 NMR (CDCl<sub>3</sub>, δ) : 1.20-1.95 (12H, m), 3.34 (3H, s),  
3.38 (2H, t, J=7Hz), 3.98 (3H, s), 4.02 (2H, t,  
J=6.5Hz), 7.00 (2H, d, J=8.7Hz), 7.59 (2H, d,  
J=8.7Hz), 7.73 (2H, d, J=8.5Hz), 8.19 (2H, d,  
J=8.5Hz), 8.22 (4H, s)

MASS (m/z) : 515 (M<sup>+</sup>)

35 Preparation 68

Methyl 4-[5-[4'-[4"-[3-(2,6-dimethylmorphino)-  
propyloxy]phenyl]phenyl]-1,3,4-oxadiazol-2-yl]benzoate

NMR (CDCl<sub>3</sub>, δ) : 1.26 (6H, d, J=6.3Hz), 2.32-2.60 (4H,  
m), 3.15-3.30 (2H, m), 3.43 (2H, d, J=11.1Hz), 3.98  
5 (3H, s), 4.10-4.20 (2H, m), 4.30-4.50 (2H, m), 6.98  
(2H, d, J=8.7Hz), 7.61 (2H, d, J=8.8Hz), 7.73 (2H,  
d, J=8.5Hz), 8.20 (2H, d, J=8.5Hz), 8.23 (4H, s)

MASS (m/z) : 528 (M<sup>+</sup>)

The following compound was obtained in a manner similar  
10 to that of Preparation 9.

Preparation 69

Methyl 4-[5-(1-n-decylpyrazol-4-yl)-1,3,4-thiadiazol-  
2-yl]benzoate

NMR (DMSO-d<sub>6</sub>, δ) : 0.84 (3H, br s), 1.23 (14H, br s),  
15 1.70-1.90 (2H, m), 3.90 (3H, s), 4.15-4.23 (2H, m),  
8.09 (1H, s), 8.13 (4H, s), 8.58 (1H, s)

MASS (m/z) : 427 (M<sup>+</sup>)

The following compound was obtained in a manner similar  
to that of Preparation 1.

20 Preparation 70

Methyl 4-[4'-(3-bromopropyloxy)phenyl]benzoate

NMR (DMSO-d<sub>6</sub>, δ) : 2.22-2.32 (2H, m), 3.69 (2H, t,  
J=6.6Hz), 3.87 (3H, s), 4.15 (2H, t, J=6Hz), 7.08  
(2H, d, J=8.8Hz), 7.71 (2H, d, J=8.7Hz), 7.79 (2H,  
25 d, J=8.5Hz), 8.01 (2H, d, J=8.4Hz)

The following compound was obtained in a manner similar  
to that of Preparation 19.

Preparation 71

1-(4-Cyclohexyloxybenzoyl)-3-thiosemicarbazide

30 NMR (DMSO-d<sub>6</sub>, δ) : 1.32 (6H, m), 1.71 (2H, m), 1.91  
(2H, m), 4.45 (1H, m), 7.00 (2H, d, J=8.8Hz), 7.57  
(2H, s), 7.84 (2H, d, J=8.7Hz), 9.27 (1H, s), 10.21  
(1H, s)

MASS (m/z) : 294 (M<sup>+</sup>+1)

35 The following compound was obtained in a manner similar

to that of Preparation 21.

Preparation 72

2-Amino-5-(4-cyclohexyloxyphenyl)-1,3,4-thiadiazole

IR (KBr) : 3272.6, 3114.5, 2937.1, 2856.1, 1604.5,

5 1519.6, 1465.6  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.17-1.48 (6H, m), 1.73 (2H, m),

1.92 (2H, m), 4.40 (1H, m), 7.00 (2H, d,  $J=8.8\text{Hz}$ ),

7.27 (2H, s), 7.64 (2H, d,  $J=8.8\text{Hz}$ )

MASS (m/z) : 276 ( $\text{M}^+ + 1$ )

10 The following compound was obtained in a manner similar to that of Preparation 23.

Preparation 73

4-[2-(4-Cyclohexyloxyphenyl)imidazo[2,1-b][1,3,4]-thiadiazol-6-yl]benzoic acid ethyl ester trifluoroacetate

15 IR (KBr) : 2931.3, 2861.8, 1714.4, 1702.8, 1502.3,

1280.5, 1257.4  $\text{cm}^{-1}$

MASS (m/z) : 448 ( $\text{M}^+ + 1$ )

The following compound was obtained in a manner similar to that of Preparation 25.

20 Preparation 74

4-[2-(4-Cyclohexyloxyphenyl)imidazo[2,1-b][1,3,4]-thiadiazol-6-yl]benzoic acid

IR (KBr) : 2931.3, 1679.7, 1606.4, 1473.3, 1421.3,

1290.1, 1249.6  $\text{cm}^{-1}$

25 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.43 (6H, m), 1.74 (2H, m), 1.94

(2H, m), 4.50 (1H, m), 7.14 (2H, d,  $J=8.8\text{Hz}$ ), 7.88

(2H, d,  $J=8.8\text{Hz}$ ), 8.00 (4H, s), 8.86 (1H, s)

MASS (m/z) : 420 ( $\text{M}^+ + 1$ )

30 The following compounds [Preparations 75 to 84] were obtained in a manner similar to that of Preparation 5.

Preparation 75

4-(4'-Methoxyphenyl)benzoylhydrazine

IR (KBr) : 3292, 3205, 1655, 1622  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.59 (2H, br), 3.86 (3H, s), 6.99

35 (2H, d,  $J=7.9\text{Hz}$ ), 7.38 (1H, br), 7.55 (2H, d,

J=7.9Hz), 7.62 (2H, d, J=7.3Hz), 7.79 (2H, d, J=7.3Hz)

MASS (m/z) : 243 ( $M^+ + 1$ )

Preparation 76

5 4-(4'-Butyloxyphenyl)benzoylhydrazine

IR (KBr) : 3340, 3277, 3194, 2956, 2918, 2870, 1655,  
1610  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.99 (3H, t, J=7.3Hz), 1.53 (4H, m),  
1.80 (2H, tt, J=6.4 and 6.4Hz), 4.02 (2H, t, J=6.4Hz),  
10 6.98 (2H, d, J=8.8Hz), 7.38 (1H, s), 7.54 (2H, d,  
J=8.8Hz), 7.62 (2H, d, J=8.4Hz), 7.79 (2H, d,  
J=8.4Hz)

MASS (m/z) : 285 ( $M^+ + 1$ )

Preparation 77

15 4-(4'-n-Pentyloxyphenyl)benzoylhydrazine

IR (KBr) : 3288, 3205, 3059, 2958, 2937, 2868, 1655,  
1622, 1601  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.94 (3H, t, J=6.8Hz), 1.44 (4H, m),  
1.60 (2H, br), 1.82 (2H, m), 4.00 (2H, t, J=6.8Hz),  
20 6.98 (2H, t, J=8.5Hz), 7.38 (1H, br), 7.54 (2H, d,  
J=8.5Hz), 7.62 (2H, d, J=8.1Hz), 7.79 (2H, d,  
J=8.1Hz)

MASS (m/z) : 299 ( $M^+ + 1$ )

Preparation 78

25 4-(4'-n-Hexyloxyphenyl)benzoylhydrazine

IR (KBr) : 3288, 3207, 3057, 2954, 2935, 2868, 1655,  
1626, 1606  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, m), 1.36 (6H, m), 1.81 (2H,  
m), 4.01 (2H, m), 6.98 (2H, d, J=8.0Hz), 7.20 (1H,  
30 br), 7.54 (2H, d, J=8.0Hz), 7.62 (2H, d, J=7.9Hz),  
7.78 (2H, d, J=7.9Hz)

MASS (m/z) : 313 ( $M^+ + 1$ )

Preparation 79

35 4-(4'-n-Heptyloxyphenyl)benzoylhydrazine

IR (KBr) : 3286, 3205, 3061, 2956, 2931, 2856, 1654,



1623, 1608  $\text{cm}^{-1}$ 

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, m), 1.32 (8H, m), 1.81 (2H, m), 4.00 (2H, m), 6.98 (2H, d,  $J=8.4\text{Hz}$ ), 7.40 (1H, br), 7.52 (2H, d,  $J=8.4\text{Hz}$ ), 7.64 (2H, d,  $J=8.4\text{Hz}$ ), 7.77 (2H, d,  $J=8.4\text{Hz}$ )

MASS (m/z) : 327 ( $\text{M}^++1$ )Preparation 80

4-[4'-[3-(Piperazin-1-yl)propyloxy]phenyl]-benzoylhydrazine

IR (KBr) : 3275, 3105, 3041, 2956, 2933, 2870, 2852, 2814, 2767, 1643  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.47 (2H, m), 1.63 (4H, m), 2.03 (2H, tt,  $J=6.3\text{Hz}$ ), 2.50 (6H, m), 4.06 (2H, t,  $J=6.3\text{Hz}$ ), 6.98 (2H, d,  $J=8.8\text{Hz}$ ), 7.41 (1H, s), 7.54 (2H, d,  $J=8.8\text{Hz}$ ), 7.62 (2H, d,  $J=8.5\text{Hz}$ ), 7.79 (2H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 354 ( $\text{M}^++1$ )Preparation 81

1-n-Decyl-4-pyrazolylcarbonylhydrazine

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.82-0.95 (3H, m), 1.22 (14H, br s), 1.62-1.81 (2H, m), 4.08 (2H, t,  $J=6.9\text{Hz}$ ), 4.29 (2H, d,  $J=4\text{Hz}$ ), 7.82 (1H, s), 8.12 (1H, s), 9.28 (1H, br s)

MASS (m/z) : 267 ( $\text{M}^+$ )Preparation 82

4-[4'-(3-Phenoxypropyloxy)phenyl]benzoylhydrazine

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 2.16-2.26 (2H, m), 4.11-4.23 (4H, m), 4.54 (2H, s), 6.89-6.98 (3H, m), 7.06 (2H, d,  $J=8.8\text{Hz}$ ), 7.25-7.33 (2H, m), 7.67 (2H, d,  $J=8.7\text{Hz}$ ), 7.70 (2H, d,  $J=8.4\text{Hz}$ ), 7.89 (2H, d,  $J=8.4\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 363 ( $\text{M}^+$ )Preparation 83

4-[4'-Allyloxyphenyl]benzoylhydrazine

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 4.51 (2H, s), 4.60-4.65 (2H, m),

5.25-5.47 (2H, m), 5.98-6.17 (1H, m), 7.06 (2H, d, J=8.8Hz), 7.67 (2H, d, J=8.8Hz), 7.70 (2H, d, J=8.4Hz), 7.89 (2H, d, J=8.4Hz), 9.80 (1H, s)

MASS (m/z) : 269 (M<sup>+</sup>)

5 Preparation 84

4-[4'-[3-(2,6-Dimethylmorpholino)propyloxy]phenyl]-benzoylhydrazine

NMR (DMSO-d<sub>6</sub>, δ) : 1.04 (6H, d, J=6.3Hz), 1.58 (2H, t, J=10.6Hz), 1.86-1.92 (2H, m), 2.40 (2H, t, J=7Hz),  
10 2.75 (2H, d, J=10.2Hz), 3.51-3.58 (2H, m), 4.05 (2H, t, J=6.2Hz), 4.50 (2H, s), 7.02 (2H, d, J=8.8Hz), 7.64-7.71 (4H, m), 7.88 (2H, d, J=8.4Hz), 9.79 (1H, s)

MASS (m/z) : 384 (M<sup>+</sup>)

15 The following compounds [Preparations 85 to 96] were obtained in a manner similar to that of Preparation 7.

Preparation 85

1-[4-(4'-Methoxyphenyl)benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

20 IR (KBr) : 3228, 2956, 2840, 1720, 1680, 1655 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 3.82 (3H, s), 3.90 (3H, s), 7.06 (2H, d, J=8.8Hz), 7.72 (2H, d, J=8.8Hz), 7.79 (2H, d, J=8.5Hz), 8.00 (2H, d, J=8.5Hz), 8.05 (2H, d, J=8.7Hz), 8.11 (2H, d, J=8.7Hz), 10.60 (1H, s),  
25 10.72 (1H, s)

MASS (m/z) : 405 (M<sup>+</sup>+1)

Preparation 86

1-[4-(4'-Butyloxyphenyl)benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

30 IR (KBr) : 3242, 3088, 3028, 2956, 2933, 2872, 1724, 1682, 1655, 1605 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, t, J=7.3Hz), 1.45 (2H, qt, J=7.3 and 6.4Hz), 1.73 (2H, tt, J=6.4 and 6.4Hz), 3.91 (3H, s), 4.03 (2H, t, J=6.4Hz), 7.05 (2H, d, J=8.8Hz), 7.70 (2H, d, J=8.8Hz), 7.90 (2H, d,  
35

J=8.4Hz), 8.00 (2H, d, J=8.4Hz), 8.05 (2H, d, J=8.4Hz), 8.05 (2H, d, J=8.7Hz), 8.11 (2H, d, J=8.7Hz), 10.60 (1H, s), 10.72 (1H, s)

MASS (m/z) : 447 (M<sup>+</sup>+1)

5 Preparation 87

1-[4-(4'-Pentyloxyphenyl)benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3226, 3030, 2958, 2931, 2870, 1724, 1680, 1655, 1605 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=6.7Hz), 1.40 (4H, m), 1.74 (2H, m), 3.90 (3H, s), 4.03 (2H, t, J=6.5Hz), 7.05 (2H, d, J=8.6Hz), 7.70 (2H, d, J=8.6Hz), 7.78 (2H, d, J=8.3Hz), 8.00 (2H, d, J=8.3Hz), 8.07 (2H, d, J=8.6Hz), 8.09 (2H, d, J=8.6Hz), 10.60 (1H, s), 15 10.72 (1H, s)

MASS (m/z) : 461 (M<sup>+</sup>+1)

Preparation 88

1-[4-(4'-n-Hexyloxyphenyl)benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

20 IR (KBr) : 3242, 3219, 3091, 3028, 2956, 2933, 2866, 1724, 1680, 1655, 1605 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.89 (3H, t, J=6.2Hz), 1.35 (6H, m), 1.74 (2H, m), 3.90 (3H, s), 4.03 (2H, t, J=6.9Hz), 7.05 (2H, d, J=8.7Hz), 7.70 (2H, d, J=8.7Hz), 7.79 (2H, d, J=8.3Hz), 8.00 (2H, d, J=8.3Hz), 8.06 (2H, d, J=8.6Hz), 8.10 (2H, d, J=8.6Hz), 10.60 (1H, s), 25 10.72 (1H, s)

MASS (m/z) : 475 (M<sup>+</sup>+1)

Preparation 89

30 1-[4-(4'-n-Heptyloxyphenyl)benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3219, 3091, 3029, 2956, 2931, 2856, 1722, 1679, 1652, 1604 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.88 (3H, br), 1.29 (8H, br), 1.75 (2H, br), 3.90 (3H, s), 4.02 (2H, br), 7.03 (2H, d, 35

J=8.4Hz), 7.70 (2H, d, J=8.4Hz), 7.80 (2H, d, J=8.8Hz), 8.00 (2H, d, J=8.8Hz), 8.45 (2H, br)

MASS (m/z) : 489 ( $M^+$ +1)

Preparation 90

5 1-[4-[4'-[3-(Piperidin-1-yl)propyloxy]phenyl]-benzoyl]-2-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3061, 3026, 2933, 2852, 2805, 2771, 2391, 1724  $\text{cm}^{-1}$

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.49 (6H, m), 1.88 (2H, tt, J=6.2 and 6.2Hz), 2.36 (6H, m), 3.90 (3H, s), 4.06 (2H, t, J=6.2Hz), 7.05 (2H, d, J=8.7Hz), 7.70 (2H, d, J=8.7Hz), 7.78 (2H, d, J=8.4Hz), 8.00 (2H, d, J=8.4Hz), 8.05 (2H, d, J=8.5Hz), 8.11 (2H, d, J=8.5Hz), 10.6 (1H, s)

15 MASS (m/z) : 516 ( $M^+$ +1)

Preparation 91

N-(4-Methoxycarbonylbenzoyl)-N'-(1-n-decyl-4-pyrazolylcarbonyl)hydrazine

20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.82-0.89 (3H, m), 1.24 (14H, br s), 1.70-1.90 (2H, m), 3.90 (3H, s), 4.14 (2H, t, J=7Hz), 7.95 (1H, s), 8.02 (2H, d, J=8.5Hz), 8.10 (2H, d, J=8.5Hz), 8.28 (1H, s), 10.18 (1H, s), 10.50 (1H, s)

MASS (m/z) : 429 ( $M^+$ )

25 Preparation 92

N-[4-[4'-(3-Phenoxypropyloxy)phenyl]benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine

30 IR (KBr) : 3210.9, 1724.0, 1650.8, 1602.6, 1560.1, 1523.5, 1502.3, 1469.5, 1432.9, 1284.4, 1247.7  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 2.18-2.24 (2H, m), 3.90 (3H, s), 4.13-4.21 (4H, m), 6.95-6.99 (3H, m), 7.09 (2H, d, J=7.9Hz), 7.25-7.33 (2H, m), 7.69-7.81 (4H, m), 7.98-8.09 (6H, m), 10.61 (1H, s), 10.73 (1H, s)

35 MASS (m/z) : 525 ( $M^+$ )

Preparation 93

N-[4-(4'-Allyloxyphenyl)benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3228.3, 3023.8, 1724.0, 1679.7, 1654.6,  
5 1604.5, 1554.3, 1513.8, 1492.6, 1434.8  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.90 (3H, s), 4.64 (2H, d,  $J=5.1\text{Hz}$ ),  
5.26-5.47 (2H, m), 5.98-6.17 (1H, m), 7.08 (2H, d,  
 $J=8.7\text{Hz}$ ), 7.72 (2H, d,  $J=8.7\text{Hz}$ ), 7.80 (2H, d,  
 $J=8.4\text{Hz}$ ), 8.00 (2H, d,  $J=8.5\text{Hz}$ ), 8.05 (2H, d,  
10  $J=8.6\text{Hz}$ ), 8.11 (2H, d,  $J=8.6\text{Hz}$ ), 10.60 (1H, s),  
10.72 (1H, s)

MASS (m/z) : 431 ( $\text{M}^+$ )

Preparation 94

15 N-[4-[4'-(4-Phenoxybutyloxy)phenyl]benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 3228.3, 1724.0, 1679.7, 1654.6,  
1602.6  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.90 (4H, br s), 3.90 (3H, s),  
4.05-4.11 (4H, m), 6.88-6.96 (3H, m), 7.05-7.09 (2H,  
20 m), 7.25-7.28 (2H, m), 7.69-8.09 (10H, m), 10.60 (1H,  
s), 10.72 (1H, s)

Preparation 95

25 N-[4-[4'-[3-(2,6-Dimethylmorpholino)propyloxy]-phenyl]benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine

IR (KBr) : 1720.2, 1681.6, 1645.0, 1604.5  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.05 (6H, d,  $J=6.3\text{Hz}$ ), 1.53-1.64  
(2H, m), 1.87-1.93 (2H, m), 2.41 (2H, t,  $J=7.1\text{Hz}$ ),  
2.76 (2H, d,  $J=10.4\text{Hz}$ ), 3.52-3.59 (2H, m), 3.90 (3H,  
s), 4.00-4.10 (2H, m), 7.05 (2H, d,  $J=8.7\text{Hz}$ ), 7.71  
30 (2H, d,  $J=8.7\text{Hz}$ ), 7.79 (2H, d,  $J=8.4\text{Hz}$ ), 8.00 (2H,  
d,  $J=8.6\text{Hz}$ ), 8.02-8.13 (4H, m), 10.60 (1H, s), 10.72  
(1H, s)

MASS (m/z) : 546 ( $\text{M}^+$ )

Preparation 96

35 N-[6-(1-Piperidyl)nicotinoyl]-N'-(4-methoxycarbonyl-

benzoyl)hydrazine

IR (KBr) : 3240, 2933, 2852, 1724, 1686, 1643, 1603,  
1547, 1497, 1437  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.4-1.7 (6H, m), 3.6-3.7 (4H, m),  
3.90 (3H, s), 6.92 (1H, d,  $J=9.0\text{Hz}$ ), 7.9-8.2 (5H,  
m), 8.65 (1H, s), 10.34 (1H, s), 10.62 (1H, s)

MASS (m/z) : 383 ( $\text{M}^++1$ )

The following compounds [Preparations 97 to 108] were  
obtained in a manner similar to that of Preparation 11.

10 Preparation 97

4-[5-[4'-(4''-(8-Methoxy-n-octyloxy)phenyl)phenyl]-  
1,3,4-oxadiazol-2-yl]benzoic acid

15 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.20-1.60 (10H, m), 1.60-1.80 (2H,  
m), 3.21 (3H, s), 3.25-3.50 (3H, m), 3.90-4.10 (2H,  
m), 6.95-7.10 (2H, m), 7.50-7.80 (4H, m), 7.80-8.00  
(2H, m), 8.10-8.30 (4H, m)

MASS (m/z) : 501 ( $\text{M}^+$ )

Preparation 98

20 4-[5-[4'-(4''-Methoxyphenyl)phenyl]-1,3,4-oxadiazol-2-  
yl]benzoic acid

IR (KBr) : 2960, 2904, 2839, 2675, 2543, 1684,  
1604  $\text{cm}^{-1}$

25 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.83 (3H, s), 7.08 (2H, d,  $J=8.5\text{Hz}$ ),  
7.91 (2H, d,  $J=8.5\text{Hz}$ ), 8.17 (2H, d,  $J=8.5\text{Hz}$ ), 8.20  
(2H, d,  $J=8.5\text{Hz}$ ), 8.28 (2H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 373 ( $\text{M}^++1$ )

Preparation 99

30 4-[5-[4'-(4''-Butyloxyphenyl)phenyl]-1,3,4-oxadiazol-  
2-yl]benzoic acid

IR (KBr) : 2958, 2935, 2871, 1687  $\text{cm}^{-1}$

35 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.3\text{Hz}$ ), 1.46 (2H, qt,  
 $J=7.3$  and  $7.5\text{Hz}$ ), 1.73 (2H, tt,  $J=7.5$  and  $6.3\text{Hz}$ ),  
4.04 (2H, t,  $J=6.3\text{Hz}$ ), 7.07 (2H, d,  $J=8.9\text{Hz}$ ), 7.75  
(2H, d,  $J=8.9\text{Hz}$ ), 7.91 (2H, d,  $J=8.4\text{Hz}$ ), 8.16 (2H,  
d,  $J=8.3\text{Hz}$ ), 8.20 (2H, d,  $J=8.3\text{Hz}$ ), 8.28 (2H, d,

J=8.4Hz)

MASS (m/z) : 415 ( $M^+ + 1$ )

Preparation 100

5 4-[5-[4'-(4"-Pentyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid

IR (KBr) : 2958, 2933, 2865, 2673, 2546, 1685  $\text{cm}^{-1}$

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.91 (3H, t, J=7.0Hz), 1.40 (4H, m), 1.75 (2H, tt, J=6.6 and 6.6Hz), 4.04 (2H, t, J=6.6Hz), 7.07 (3H, d, J=8.8Hz), 7.74 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.5Hz), 8.15 (2H, d, J=8.4Hz), 8.20 (2H, d, J=8.1Hz), 8.27 (2H, d, J=8.5Hz)

MASS (m/z) : 429 ( $M^+ + 1$ )

Preparation 101

15 4-[5-[4'-(4"-Hexyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid

IR (KBr) : 2954, 2933, 2864, 2675, 2546, 1686  $\text{cm}^{-1}$

20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t, J=6.8Hz), 1.30 (6H, m), 1.74 (2H, tt, J=7.7 and 6.4Hz), 4.04 (2H, t, J=6.4Hz), 7.07 (2H, d, J=8.8Hz), 7.74 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.0Hz), 8.16 (2H, d, J=8.6Hz), 8.20 (2H, d, J=8.0Hz), 8.27 (2H, d, J=8.6Hz)

MASS (m/z) : 433 ( $M^+ + 1$ )

Preparation 102

25 4-[5-[4'-(4"-n-Heptyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid

IR (KBr) : 2956, 2931, 2856, 2671, 2545, 1686  $\text{cm}^{-1}$

MASS (m/z) : 457 ( $M^+ + 1$ )

Preparation 103

30 4-[5-(1-n-Decylpyrazol-4-yl)-1,3,4-oxadiazol-2-yl]benzoic acid

35 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.75-0.95 (3H, m), 1.23 (14H, br s), 1.83 (2H, br s), 3.33 (1H, br s,  $\text{CO}_2\text{H}$ ), 4.22 (2H, t, J=6.8Hz), 8.14 (1H, s), 8.17 (4H, s), 8.65 (1H, s)

MASS (m/z) : 397 ( $M^+$ )

Preparation 104

4-[5-[1-n-Decylpyrazol-4-yl]-1,3,4-thiadiazol-2-yl]-  
benzoic acid

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.80-0.90 (3H, m), 1.23 (14H, br s),  
1.70-1.90 (2H, m), 3.34 (1H, br s), 4.19 (2H, t,  
J=6.9Hz), 8.08 (1H, s), 8.10 (4H, s), 8.58 (1H, s)

Preparation 105

10 4-[5-[4'-[4''-(3-Phenoxypropyloxy)phenyl]phenyl]-  
1,3,4-oxadiazol-2-yl]benzoic acid

IR (KBr) : 1685.5, 1602.6, 1548.6, 1490.7, 1469.5,  
1429.0, 1400.1, 1290.1, 1249.6  $cm^{-1}$

15 NMR (DMSO- $d_6$ ,  $\delta$ ) : 2.18-2.24 (2H, m), 4.13-4.25 (4H,  
m), 6.90-6.99 (3H, m), 7.11 (2H, d, J=8.8Hz),  
7.26-7.33 (2H, m), 7.75 (2H, d, J=8.7Hz), 7.91 (2H,  
d, J=8.5Hz), 8.15-8.30 (6H, m), 13.20-13.60 (1H, br)

MASS (m/z) : 493 ( $M^+$ )

Preparation 106

20 4-[5-[4'-[4''-Allyloxyphenyl]phenyl]-1,3,4-oxadiazol-  
2-yl]benzoic acid

IR (KBr) : 1685.5, 1652.7, 1604.5, 1577.5, 1548.6,  
1488.8, 1429.0, 1288.2, 1253.5, 823.5  $cm^{-1}$

25 NMR (DMSO- $d_6$ ,  $\delta$ ) : 4.65 (2H, d, J=5Hz), 5.27-5.48 (2H,  
m), 5.99-6.15 (1H, m), 7.10 (2H, d, J=8.7Hz), 7.75  
(2H, d, J=8.6Hz), 7.91 (2H, d, J=8.3Hz), 8.15-8.30  
(6H, m), 12.38 (1H, br s)

MASS (m/z) : 399 ( $M^+$ )

Preparation 107

30 4-[5-[4'-[4''-(4-Phenoxybutyloxy)phenyl]phenyl]-1,3,4-  
oxadiazol-2-yl]benzoic acid

IR (KBr) : 1733.7, 1697.1, 1650.8, 1602.6  $cm^{-1}$

35 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.91 (4H, br s), 3.33 (1H, br s),  
4.05-4.12 (4H, m), 6.88-6.96 (2H, m), 7.07-7.11 (2H,  
m), 7.25-7.28 (2H, m), 7.66-8.00 (5H, m), 8.14-8.36  
(6H, m)



Preparation 108

4-[5-[4'-(4''-[3-(2,6-Dimethylmorpholino)propyloxy]-phenyl)]phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid

MASS (m/z) : 514 ( $M^+$ )

5 The following compounds [Preparations 109 to 123] were obtained in a manner similar to that of Preparation 13.

Preparation 109

4-[5-[4'-(4''-Methoxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

10 IR (KBr) : 1782  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.89 (3H, s), 7.03 (2H, d,  $J=8.7\text{Hz}$ ),  
7.53 (3H, m), 7.62 (2H, d,  $J=8.7\text{Hz}$ ), 7.76 (2H, d,  
 $J=8.4\text{Hz}$ ), 8.13 (1H, d,  $J=8.2\text{Hz}$ ), 8.23 (2H, d,  
 $J=8.4\text{Hz}$ ), 8.41 (2H, d,  $J=8.4\text{Hz}$ ), 8.48 (2H, d,  
15  $J=8.7\text{Hz}$ )

MASS (m/z) : 490 ( $M^++1$ )

Preparation 110

4-[5-[4'-(4''-Butyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

20 IR (KBr) : 2956, 2933, 2872, 1776  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00 (3H, t,  $J=7.3\text{Hz}$ ), 1.52 (2H, qt,  
 $J=7.3$  and  $6.4\text{Hz}$ ), 1.79 (2H, tt,  $J=6.4$  and  $6.4\text{Hz}$ ),  
4.04 (2H, t,  $J=6.4\text{Hz}$ ), 7.02 (2H, d,  $J=8.7\text{Hz}$ ),  
7.45-7.57 (3H, m), 7.61 (2H, d,  $J=8.7\text{Hz}$ ), 7.76 (2H,  
25 d,  $J=8.4\text{Hz}$ ), 8.14 (1H, d,  $J=8.2\text{Hz}$ ), 8.22 (2H, d,  
 $J=8.4\text{Hz}$ ), 8.40 (2H, d,  $J=8.7\text{Hz}$ ), 8.47 (2H, d,  
 $J=8.7\text{Hz}$ )

MASS (m/z) : 532 ( $M^++1$ )

Preparation 111

30 4-[5-[4'-(4''-n-Pentyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 2956, 2935, 2868, 1779  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=6.9\text{Hz}$ ), 1.44 (4H, m),  
1.77 (2H, m), 4.03 (2H, t,  $J=6.5\text{Hz}$ ), 7.02 (2H, d,  
35  $J=8.7\text{Hz}$ ), 7.45-7.57 (3H, m), 7.60 (2H, d,  $J=8.7\text{Hz}$ ),

7.75 (2H, d, J=8.4Hz), 8.14 (1H, d, J=8.2Hz), 8.22 (2H, d, J=8.4Hz), 8.22 (2H, d, J=8.4Hz), 8.40 (2H, d, J=8.7Hz), 8.47 (2H, d, J=8.7Hz)

MASS (m/z) : 546 ( $M^+$ +1)

5 Preparation 112

4-[5-[4'-(4"-n-Hexyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 2953, 2931, 2866, 1776  $\text{cm}^{-1}$

10 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (3H, t, J=6.7Hz), 1.36-1.49 (6H, m), 1.82 (2H, m), 4.03 (2H, t, J=6.5Hz), 7.02 (2H, d, J=8.8Hz), 7.45-7.57 (3H, m), 7.61 (2H, d, J=8.8Hz), 7.76 (2H, d, J=8.4Hz), 8.14 (2H, d, J=8.2Hz), 8.22 (2H, d, J=8.4Hz), 8.41 (2H, d, J=8.8Hz), 8.48 (2H, d, J=8.8Hz)

15 MASS (m/z) : 560 ( $M^+$ +1)

Preparation 113

4-[5-[4'-(4"-n-Heptyloxyphenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 2954, 2929, 2856, 1776  $\text{cm}^{-1}$

20 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.91 (3H, m), 1.34 (8H, m), 1.75 (2H, m), 4.03 (2H, t, J=6.5Hz), 7.02 (2H, t, J=8.7Hz), 7.47-7.57 (3H, m), 7.61 (2H, d, J=8.7Hz), 7.76 (2H, d, J=8.3Hz), 8.14 (1H, d, J=8.2Hz), 8.22 (2H, d, J=8.3Hz), 8.41 (2H, d, J=8.5Hz), 8.48 (2H, d, J=8.5Hz)

25 MASS (m/z) : 574 ( $M^+$ +1)

Preparation 114

4-[5-(1-n-Decylpyrazol-4-yl)-1,3,4-oxadiazol-2-yl]-benzoic acid benzotriazol-1-yl ester

30 IR (KBr) : 1783.8, 1623.8, 1234.2, 989.3  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.84-0.91 (3H, m), 1.26-1.34 (14H, m), 1.80-2.00 (2H, m), 4.23 (2H, t, J=7.1Hz), 7.44-7.63 (3H, m), 8.11-8.15 (3H, m), 8.35 (2H, d, J=8.7Hz), 8.45 (2H, d, J=8.7Hz)

35 MASS (m/z) : 514 ( $M^+$ )

Preparation 115

4-[5-(1-n-Decylpyrazol-4-yl)-1,3,4-thiadiazol-2-yl]-  
benzoic acid benzotriazol-1-yl ester

IR (KBr) : 1776.1, 1575.6, 1234.2, 983.5  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.84-0.91 (3H, m), 1.26-1.34 (14H, m),  
1.94 (2H, br s), 4.21 (2H, t,  $J=7.1\text{Hz}$ ), 7.43-7.63  
(3H, m), 7.99 (1H, s), 8.09 (1H, s), 8.10-8.15 (1H,  
m), 8.22 (2H, d,  $J=8.5\text{Hz}$ ), 8.40 (2H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 530 ( $\text{M}^+$ )

10 Preparation 116

4-[5-[4'-[4''-(3-Phenoxypropyloxy)phenyl]phenyl]-  
1,3,4-oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 1778.0, 1602.6, 1490.7, 1471.4,  
1238.1  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.27-2.34 (2H, m), 4.16-4.26 (4H, m),  
6.91-7.05 (5H, m), 7.26-7.33 (2H, m), 7.44-7.62 (5H,  
m), 7.74 (2H, d,  $J=7.9\text{Hz}$ ), 8.13 (1H, d,  $J=8.5\text{Hz}$ ),  
8.21 (2H, d,  $J=7.9\text{Hz}$ ), 8.37-8.48 (4H, m)

MASS (m/z) : 610 ( $\text{M}^+$ )

20 Preparation 117

4-[5-[4'-[4''-Allyloxyphenyl]phenyl]-1,3,4-oxadiazol-  
2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 1776.1, 1602.6, 1488.9, 1232.3  $\text{cm}^{-1}$

25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 4.61 (2H, d,  $J=5.2\text{Hz}$ ), 5.30-5.50 (2H,  
m), 6.00-6.19 (1H, m), 7.04 (2H, d,  $J=8.7\text{Hz}$ ),  
7.44-7.63 (4H, m), 7.75 (2H, d,  $J=8.4\text{Hz}$ ), 8.11-8.30  
(4H, m), 8.38-8.49 (4H, m)

MASS (m/z) : 516 ( $\text{M}^+$ )

Preparation 118

30 4-[5-[4'-[4''-(4-Phenoxybutyloxy)phenyl]phenyl]-1,3,4-  
oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 1776.1  $\text{cm}^{-1}$

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.02 (4H, br s), 4.06-4.11 (4H, m),  
6.83-7.04 (5H, m), 7.26-7.33 (1H, m), 7.48-7.63 (6H,  
m), 7.76 (2H, d,  $J=8.4\text{Hz}$ ), 8.14 (1H, d,  $J=8.2\text{Hz}$ ),

8.22 (2H, d, J=8.3Hz), 8.41 (2H, d, J=8.7Hz), 8.48 (2H, d, J=8.7Hz)

MASS (m/z) : 624 (M<sup>+</sup>)

Preparation 119

5        4-[5-[4'-(4''-(8-Methoxy-n-octyloxy)phenyl)phenyl]-1,3,4-oxadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 2931.3, 2856.1, 1776.1 cm<sup>-1</sup>

10        NMR (CDCl<sub>3</sub>, δ) : 1.30-1.70 (10H, m), 1.70-1.90 (2H, m),  
3.34 (3H, s), 3.38 (2H, t, J=6.4Hz), 4.02 (2H, t, J=6.5Hz), 7.02 (2H, d, J=8.7Hz), 7.45-7.63 (5H, m),  
7.76 (2H, d, J=8.5Hz), 8.12-8.31 (3H, m), 8.41 (2H, d, J=8.8Hz), 8.48 (2H, d, J=8.8Hz)

MASS (m/z) : 618 (M<sup>+</sup>)

Preparation 120

15        4-[5-[4'-(4-Phenoxybutyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 3058.5, 2956.3, 2873.4, 1778.0, 1602.6,  
1236.1 cm<sup>-1</sup>

20        NMR (CDCl<sub>3</sub>, δ) : 2.0-2.1 (4H, m), 4.0-4.2 (4H, m),  
6.9-7.0 (3H, m), 7.03 (2H, d, J=8.8Hz), 7.3-7.4 (2H, m), 7.4-7.6 (3H, m), 7.99 (2H, d, J=8.8Hz), 8.13 (1H, d, J=8.2Hz), 8.25 (2H, d, J=8.6Hz), 8.42 (2H, d, J=8.6Hz)

MASS (m/z) : 564 (M<sup>+</sup>+1)

25        Preparation 121

4-[5-[4'-(5-Phenoxy-n-pentyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

IR (KBr) : 2946.7, 2871.5, 1785.8, 1600.6, 1255.4,  
1234.2 cm<sup>-1</sup>

30        NMR (CDCl<sub>3</sub>, δ) : 1.5-2.1 (6H, m), 3.9-4.2 (4H, m),  
6.8-7.1 (5H, m), 7.2-7.4 (2H, m), 7.4-7.7 (3H, m),  
7.98 (2H, d, J=8.8Hz), 8.13 (1H, d, J=8.2Hz), 8.25 (2H, d, J=8.6Hz), 8.41 (2H, d, J=8.6Hz)

MASS (m/z) : 578 (M<sup>+</sup>+1)

35        Preparation 122

4-[5-[4'-(5-Methoxy-n-pentyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester

NMR (CDCl<sub>3</sub>, δ) : 1.5-2.1 (6H, m), 3.54 (3H, s), 3.43 (2H, t, J=6.1Hz), 4.06 (2H, t, J=6.3Hz), 7.02 (2H, d, J=8.8Hz), 7.4-7.7 (3H, m), 7.98 (2H, d, J=8.8Hz), 8.13 (1H, d, J=8.2Hz), 8.25 (2H, d, J=8.5Hz), 8.41 (2H, d, J=8.5Hz)

MASS (m/z) : 516 (M<sup>+</sup>+1)

Preparation 123

4-Cyclohexyloxybenzoic acid benzotriazol-1-yl ester

IR (KBr) : 2939, 2854.1, 1776.1, 1602.6, 1508.1 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.25-1.67 (6H, m), 1.85 (2H, m), 2.01 (2H, m), 4.43 (1H, m), 7.03 (2H, d, J=7.0Hz), 7.38-7.54 (3H, m), 8.08 (1H, d, J=8.2Hz), 8.19 (2H, d, J=7.0Hz)

MASS (m/z) : 338 (M<sup>+</sup>+1)

Preparation 124

To a solution of 4-methoxybenzoic acid benzotriazol-1-yl ester (80 g) in N,N-dimethylformamide (700 ml) was added thiosemicarbazide (28 g) and the mixture was stirred for 23 hours at ambient temperature. The reaction mixture was pulverized with diisopropyl ether. The precipitate was collected by filtration to give 1-(4-methoxybenzoyl)-3-thiosemicarbazide (57 g).

Preparation 125

To a slurry of 1-(4-methoxybenzoyl)-3-thiosemicarbazide (57 g) in toluene (300 ml), was added methanesulfonic acid (25 ml) dropwise over 30 minutes at 40°C. The mixture was stirred under refluxing for 24 hours. After cooling to 10°C, the sulfonate salt was filtered and dried. The salt was placed in water, and the solution was adjusted to pH 9 with 1N sodium hydroxide and extracted with ethyl acetate. The organic layer was separated, washed with brine, dried over magnesium sulfate and evaporated under reduced pressure to give 2-amino-5-(4-methoxyphenyl)-1,3,4-thiadiazole (31.1 g).

IR (KBr) : 3251, 3114.5, 1610.3, 1525  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 3.80 (3H, s), 7.00 (2H, d,  $J=8.5\text{Hz}$ ),  
7.28 (2H, s), 7.69 (2H, d,  $J=8.5\text{Hz}$ )

MASS ( $m/z$ ) : 208 ( $M+H^+$ )

5 Preparation 126

A mixture of 4-bromobenzenethiol (6 g), 1,7-dibromoheptane (16.37 g), and potassium carbonate (8.77 g) in dimethylformamide (30 ml) was stirred at room temperature for 5.5 hours. The reaction mixture was pulverized with water and  
10 extracted with ethyl acetate. The organic layer was separated, washed with brine, dried over magnesium sulfate and evaporated under reduced pressure to give 1-bromo-4-(7-bromoheptylthio)benzene (7.62 g).

IR (KBr) : 1465.6, 1089.6, 800.3  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.37-1.88 (10H, m), 2.89 (2H, t,  $J=7.2\text{Hz}$ ),  
3.40 (2H, t,  $J=6.8\text{Hz}$ ), 7.14-7.21 (2H, m), 7.36-7.43  
(2H, m)

Preparation 127

To a solution of 1-bromo-4-(7-bromoheptylthio)benzene (5  
20 g) in methanol (25 ml) was added 28% sodium methylate in methanol (7.9 g) and the mixture was stirred under refluxing for 2 hours. The reaction mixture was evaporated under reduced pressure. The residue was adjusted to pH 2 with dilute HCl aq. and extracted with ethyl acetate. The organic layer was  
25 separated, washed with brine, dried over magnesium sulfate and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with n-hexane/ethyl acetate (50:1) to give 1-bromo-4-(7-methoxyheptylthio)benzene (3.59 g).

30 IR (KBr) : 1471.4, 1118.5, 1093.4  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.30-1.67 (10H, m), 2.88 (2H, t,  $J=7.3\text{Hz}$ ),  
3.33 (3H, s), 3.36 (2H, t,  $J=6.2\text{Hz}$ ), 7.13-7.20 (2H,  
m), 7.35-7.42 (2H, m)

MASS ( $m/z$ ) : 317.1

Preparation 128

To a solution of 4-(4-chlorophenyl)-4-hydroxypiperidine (5.0 g) in dichloromethane (50 ml) was added di-tert-butyl dicarbonate (5.7 g). After stirring for 5 hours at room temperature, the solvent was evaporated in vacuo and the residue was poured into a mixture of ethyl acetate and water. The organic layer was successively washed with brine and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was purified by column chromatography on silica gel eluting with a mixture of hexane and ethyl acetate (3:1). The eluted fractions containing the desired product were collected and evaporated in vacuo to give 1-tert-butoxycarbonyl-4-(4-chlorophenyl)-4-hydroxypiperidine (7.58 g).

IR (Film) : 2976, 2926, 1668  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.47 (9H, s), 1.6-1.8 (3H, m), 1.9-2.1 (2H, m), 3.1-3.3 (2H, m), 3.9-4.1 (2H, m), 7.2-7.5 (4H, m)  
(+) APCI MS : 212 (M+H)<sup>+</sup>-101

Preparation 129

To a solution of 1-tert-butoxycarbonyl-4-(4-chlorophenyl)-4-hydroxypiperidine (1.0 g) in N,N-dimethyl formamide (10 ml) was added sodium hydride (0.14 g) under ice cooling. Then the reaction mixture was stirred for 30 minutes at room temperature and for 2 hours at 60°C. To the reaction mixture was added iodomethane (4.0 ml) at 60°C. After stirring for 6 hours at 60°C, the reaction mixture was poured into a mixture of ethyl acetate and water. The organic layer was successively washed with brine and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was purified by column chromatography on silica gel eluting with a mixture of hexane and ethyl acetate (10:1). The eluted fractions containing the desired product were collected and evaporated in vacuo to give 1-tert-butoxycarbonyl-4-(4-chlorophenyl)-4-methoxypiperidine (0.75 g).

IR (Film) : 2976, 2935, 1680  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.47 (9H, s), 1.7-2.1 (4H, m), 2.97 (3H, s), 3.0-3.3 (2H, m), 3.9-4.1 (2H, m), 7.2-7.4 (4H, m)

5 (+) APCI MS : 226 (M+H)<sup>+</sup>-101

Preparation 130

To a solution of 2-indanol (4 g) and triethylamine (5.8 ml) in dichloromethane (40 ml) was added dropwise with stirring methanesulfonylchloride (2.8 ml) in an ice-bath. The mixture was then stirred for 1.5 hours. The reaction mixture was added to a mixture of water and dichloromethane. The organic layer was taken and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was concentrated under reduced pressure to give methanesulfonic acid indan-2-yl ester (6.29 g).

IR (KBr) : 3029.6, 1328.7, 1162.9  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.02 (3H, s), 3.19-3.44 (4H, m), 5.48-5.58 (1H, m), 7.18-7.28 (4H, m)

MASS (m/z) : 119.2 (M-OMs+1)

20 Preparation 131

To a solution of 4-(5-amino-1,3,4-thiadiazol-2-yl)benzoic acid methyl ester trifluoroacetic acid salt (8 g) in water was added 1N sodium hydroxide and the mixture was adjusted to pH 8. The precipitate was collected by filtration to give 4-(5-amino-1,3,4-thiadiazol-2-yl)benzoic acid (5.05 g).

Preparation 132

A mixture of 1-(4-nitrophenyl)-1H-pyrazol-4-carboxylic acid methyl ester (19.44 g), Fe powder,  $\text{NH}_4\text{Cl}$ , methanol and  $\text{H}_2\text{O}$  was heated for 30 minutes at 80°C and 3 hours at 100°C. The reaction mixture was concentrated by evaporation, added into dichloromethane, and was filtered. The filtrate was extracted with water, dried over magnesium sulfate and concentrated by evaporation to give 1-(4-aminophenyl)-1H-pyrazol-4-carboxylic acid methyl ester (9.84 g).



IR (KBr) : 1701, 1521, 1248  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.86 (2H, brs), 3.90 (3H, s), 6.75 (2H, d,  $J=8.8\text{Hz}$ ), 7.45 (2H, d,  $J=8.8\text{Hz}$ ), 8.05 (1H, s), 8.26 (1H, s)

5        MASS (m/z) : 218 ( $M^+ + 1$ )

Preparation 133

A mixture of 1-(4-formylphenyl)-1H-pyrazol-4-carboxylic acid methyl ester (1.00 g), methanol (10 ml) and tetrahydrofuran (25 ml) was treated with sodium borohydride at 0°C. After 15 minutes, the mixture was diluted with ethyl acetate and washed with water. The organic layer was dried over magnesium sulfate, filtered, and concentrated by evaporation to give 1-(4-hydroxymethylphenyl)-1H-pyrazol-4-carboxylic acid methyl ester (1.04 g).

15        IR (KBr) : 1724, 1558, 1521, 1443, 1392, 1255  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.88 (3H, s), 4.76 (2H, s), 7.48 (2H, d,  $J=8.7\text{Hz}$ ), 7.69 (2H, d,  $J=8.7\text{Hz}$ ), 8.10 (1H, s), 8.41 (1H, s)

MASS (m/z) : 233 ( $M^+ + 1$ )

20        Preparation 134

A solution of 1-(4-formylphenyl)-1H-pyrazol-4-carboxylic acid methyl ester (5.0 g) in dichloromethane (100 ml) was treated with 3-chloroperbenzoic acid for 5 minutes at room temperature. The solution was heated at 50°C for 4 hours, during which period additional 3-chloroperbenzoic acid (1.87 g) was added. After concentration, methanol (150 ml) and potassium carbonate (9.00 g) were added to the residue, and the mixture was stirred for 14 hours at ambient temperature. The reaction mixture was poured into water, adjusted to pH 8 with 1N HCl and the resulting precipitate was collected by filtration to give 1-(4-hydroxyphenyl)-1H-pyrazol-4-carboxylic acid methyl ester (0.51 g).

35        IR (KBr) : 1718, 1691, 1554, 1523, 1250  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.87 (3H, s), 6.92 (2H, d,  $J=9.0\text{Hz}$ ), 7.55 (2H, d,  $J=9.0\text{Hz}$ ), 8.07 (1H, s), 8.30 (1H, s)

MASS (m/z) : 219(M<sup>+</sup>+1)

Preparation 135

A solution of 4-(4-hydroxypiperidin-1-yl)benzoic acid ethyl ester (5.4 g), silver oxide (5.31 g) and 3-bromocyclohexene (3.24 ml) in tetrahydrofuran (52 ml) was stirred for 1 day at room temperature. The reaction mixture was filtered off, and the filtrate was concentrated by evaporation under reduced pressure. To the residue was added ethyl acetate, and the resulting precipitate was collected by filtration and dried. The residue was purified by silica gel chromatography (3:2 hexane-ethyl acetate elution) to give 4-[4-(2-cyclohexenyloxy)piperidin-1-yl]benzoic acid ethyl ester (3.84 g).

NMR (CDCl<sub>3</sub>, δ) : 1.36 (3H, t, J=7.1Hz), 1.40-2.15 (10H, m), 3.00-3.20 (2H, m), 3.50-3.75 (3H, m), 3.90-4.05 (1H, m), 4.32 (2H, q, J=7.1Hz), 5.60-5.90 (2H, m), 6.86 (2H, d, J=9.1Hz), 7.90 (2H, d, J=9.1Hz)

APCI MASS : 330(M<sup>+</sup>+1)

Preparation 136

To a solution of 4-[4-(2-cyclohexenyloxy)piperidin-1-yl]benzoic acid ethyl ester (3.82 g) in methanol (80 ml) was added 10% palladium on carbon (1.0 g), and hydrogen gas at atmosphere pressure for 5 hours. The reaction mixture was filtered, and the filtrate was concentrated by evaporation under reduced pressure to give 4-(4-cyclohexyloxypiperidin-1-yl)benzoic acid ethyl ester (2.38 g).

NMR (CDCl<sub>3</sub>, δ) : 1.10-1.32 (4H, m), 1.36 (3H, t, J=7.1Hz), 1.40-2.00 (9H, m), 2.90-3.15 (2H, m), 3.20-3.45 (1H, m), 3.50-3.75 (3H, m), 4.32 (2H, q, J=7.1Hz), 6.86 (2H, dd, J=2.2 and 9.1Hz), 7.85-8.00 (2H, m)

APCI MASS (positive) : 332.3(M<sup>+</sup>+1)

Preparation 137

To a suspension of 4-[2-(4-methoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester trifluoroacetic acid salt (1.0 g) in dichloromethane (10 ml)

was added borone tribromide (1.0M solution in dichloromethane) (8.0 ml) at 0°C and the mixture was stirred at ambient temperature for 1 week. The reaction mixture was pulverized with cold water. The precipitate was collected by  
5 filtration and dried to give 4-[2-(4-hydroxyphenyl)imidazo-[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid (893 mg).

IR (KBr) : 3209, 1689.3, 1604.5, 1484.9  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 6.97 (2H, d,  $J=8.5\text{Hz}$ ), 7.81 (2H, d,  $J=8.5\text{Hz}$ ), 8.00 (4H, s), 8.84 (1H, s)

10 MASS (m/z) : 338 ( $M+H^+$ )

#### Preparation 138

To a solution of 5-(4-pentyloxyphenyl)-1,3,4-thiadiazol-2-yl-amine (20 g) in pyridine (200 ml) was added 4-methoxycarbonylbenzoylchloride (15 g) and the mixture was  
15 stirred at ambient temperature for 2 hours. The reaction mixture was pulverized with water. The precipitate was collected by filtration and dried to give N-[5-(4-pentyloxyphenyl)-1,3,4-thiadiazol-2-yl]terephthalamic acid methyl ester (30.3 g).

20 IR (KBr) : 2946, 2863, 1724, 1670, 1604, 1538, 1521, 1457, 1317, 1276, 1249, 1174, 1106  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=7.0\text{Hz}$ ), 1.2-1.5 (4H, m), 1.6-1.9 (2H, m), 3.90 (3H, s), 4.05 (2H, t,  $J=6.5\text{Hz}$ ), 7.09 (2H, d,  $J=8.8\text{Hz}$ ), 7.91 (2H, d,  $J=8.8\text{Hz}$ ), 8.12 (2H, d,  $J=8.4\text{Hz}$ ), 8.25 (2H, d,  $J=8.4\text{Hz}$ ),  
25

MASS (m/z) : 426 ( $M+H^+$ )

#### Preparation 139

To a solution of N-tert-butoxycarbonyl-4-piperidinone (3.3 g) and 1-(4-cyclohexylphenyl)piperazine (4.0 g) in  
30 dichloromethane (20 ml) was added titanium(IV)isopropoxide (8 ml) and the mixture was stirred at ambient temperature for 2 hours. Then, to the reaction mixture was added ethanol (20 ml) and sodium cyanoborohydride (1 g) in several portions, the  
35 reaction mixture was stirred at ambient temperature for 2 hours.

The reaction mixture was pulverized with water. The precipitate was filtered off and the filtrate was extracted with dichloromethane. The organic layer was taken and dried over magnesium sulfate. Magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure and chromatographed (Silica gel 60 (Trademark : prepared by Merck)) eluting with hexane/ethyl acetate to afford 1-tert-butoxycarbonyl-4-[4-(4-cyclohexylphenyl)piperazin-1-yl]piperidine (1.35 g).

NMR (CDCl<sub>3</sub>, δ) : 1.3-1.6 (6H, m), 1.45 (9H, s), 1.6-2.0 (8H, m), 2.3-2.6 (2H, m), 2.6-3.0 (6H, m), 3.0-3.3 (4H, m), 4.17 (2H, d, J=13Hz), 6.86 (2H, d, J=8.7Hz), 7.11 (2H, d, J=8.7Hz)

MASS (m/z) : 428 (M+H<sup>+</sup>)

#### Preparation 140

To a solution of 4-[4-[4-(4-cyclohexylphenyl)piperazin-1-yl]piperidin-1-yl]benzonitrile (1.95 g) in acetic acid (10 ml) was added concentrated hydrogen chloride (20 ml) and the mixture was stirred at 120°C for 10 hours. The reaction mixture was added to water and the resulting precipitate was collected by filtration to give 4-[4-[4-(4-cyclohexylphenyl)piperazin-1-yl]piperidin-1-yl]benzoic acid (959 mg).

IR (KBr) : 3400, 2927, 2620, 2514, 1714, 1608, 1513, 1452, 1274, 1226, 1182, 1010 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.2-1.5 (5H, m), 1.6-1.9 (7H, m), 2.2 (2H, m), 2.4 (1H, m), 2.84 (2H, t, J=8.5Hz), 3.20 (4H, d, J=8.5Hz), 3.4-3.8 (5H, m), 4.08 (2H, d, J=12.5Hz), 6.93 (2H, d, J=8.8Hz), 7.03 (2H, d, J=8.8Hz), 7.12 (2H, d, J=8.8Hz), 7.78 (2H, d, J=8.8Hz), 11.13 (1H, s)

MASS (m/z) : 448 (M+H<sup>+</sup>)

#### Preparation 141

A mixture of 1-(4-formylphenyl)-1H-pyrazol-4-carboxylic acid methyl ester (5.0 g), 1-phenyl piperazine (4.21 g), acetic

acid (3.7 ml), sodium cyanoborohydride (1.55 g), methanol (110 ml), tetrahydrofuran (75 ml) and dichloromethane (20 ml) was stirred for 15 minutes at 0°C and for 14 hours at ambient temperature. The reaction mixture was poured into saturated NaHCO<sub>3</sub> aqueous solution and extracted with ethyl acetate. The organic layer was dried over magnesium sulfate, filtered, and evaporated. The residue was purified by silica gel chromatography (1:1 hexane-ethyl acetate elution) and recrystallized from diisopropyl ether and acetone to give 1-[4-(4-phenylpiperazin-1-yl-methyl)phenyl]-1H-pyrazol-4-carboxylic acid methyl ester (3.90 g).

IR (KBr) : 1702, 1600, 1560, 1271 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 2.4-2.6 (4H, m), 3.14 (3H, t, J=4.8Hz), 3.58 (2H, s), 3.81 (3H, s), 6.76 (1H, t, J=7.2Hz), 6.91 (2H, d, J=7.8Hz), 7.20 (2H, t, J=7.8Hz), 7.48 (2H, t, J=8.6Hz), 7.90 (2H, d, J=8.6Hz), 8.15 (1H, s), 9.11 (1H, s)

MASS (m/z) : 377 (M<sup>+</sup>+1)

#### Preparation 142

To an ice-cooled solution of methyl 4-(4-hydroxyphenyl)benzoate (3.00 g) and N-phenyltrifluoromethanesulfonide (4.84 g) in tetrahydrofuran (60 ml) was added triethylamine (1.98 ml), then the solution was stirred at this temperature for 1 hour and at ambient temperature for further 18 hours. Water (200 ml) was added to the reaction mixture and the mixture was extracted with methylene chloride. The organic layer was dried over magnesium sulfate, filtered and evaporated to give a crude oil. This oil was purified on a silica gel column chromatography eluting successively with the following solvents: (1) 2.5% ethyl acetate in n-hexane, (2) 5% ethyl acetate in n-hexane. The fractions containing the object compound were concentrated to give methyl 4-(4-trifluoromethanesulfonyloxyphenyl)-benzoate (5.30 g) as a white solid.

IR (KBr) : 1713, 1691, 1606, 1522, 1495, 1420 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 3.95 (3H, s), 7.31-7.46 (2H, m), 7.56-7.75 (4H, m), 8.08-8.20 (2H, m)

MASS (m/z) : 361 (M<sup>+</sup>+1)

#### Preparation 143

5 To a suspension of 4-piperazin-1-yl-benzoic acid ethyl ester dihydrochloride (1 g) and potassium bicarbonate (1.57 g) in acetonitrile (10 ml) was added methanesulfonic acid indane-2-yl ester (0.69 g) and the mixture was stirred under refluxing for 8 hours. The reaction mixture was pulverized  
10 with water. The precipitate was collected by filtration and dried over under reduced pressure. The powder was purified by column chromatography on silica gel using methanol/dichloromethane (50:1) as the eluent to give 4-(4-indan-2-yl-piperazin-1-yl)benzoic acid ethyl ester (0.38  
15 g).

IR (KBr) : 1697.1, 1606.4, 1349.9, 1238.1 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.37 (3H, t, J=7.1Hz), 2.67-2.72 (4H, m), 2.88-3.40 (9H, m), 4.33 (2H, q, J=7.1Hz), 6.85-6.90 (2H, m), 7.12-7.23 (4H, m), 7.91-7.96 (2H, m)  
20

MASS (m/z) : 351.3 (M+1)

#### Preparation 144

To a solution of 2-amino-4'-bromoacetophenone hydrochloride (5.0 g), 4-heptyloxybenzoic acid (4.72 g) and  
25 1-hydroxybenzotriazole (2.7 g) in dichloromethane (50 ml) was added 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide (WSCD) (3.65 ml) and the mixture was stirred for 3 hours at ambient temperature. The reaction mixture was diluted with dichloromethane (200 ml), and washed with water, 1N  
30 hydrochloric acid, saturated sodium hydrogen carbonate aqueous solution and brine. The organic layer was dried over magnesium sulfate. Magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure. The solids were slurried in ethyl acetate and collected by  
35 filtration to give 2-(4-heptyloxybenzoylamino)-4'-

bromoacetophenone (6.73 g).

IR (KBr) : 3318.9, 2937.1, 2858.0, 1699.0, 1639.2,  
1556.3, 1508.1, 1255.4  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.80-1.10 (3H, m), 1.20-1.60 (8H, m),  
1.75-1.95 (2H, m), 4.01 (2H, t,  $J=6.5\text{Hz}$ ), 4.91 (2H,  
d,  $J=4.2\text{Hz}$ ), 6.94 (2H, d,  $J=8.8\text{Hz}$ ), 7.14 (1H, brs),  
7.67 (2H, d,  $J=8.6\text{Hz}$ ), 7.83 (2H, d,  $J=8.8\text{Hz}$ ), 7.90  
(2H, d,  $J=8.6\text{Hz}$ )

APCI-MS ( $m/z$ ) : 432, 434

10 Preparation 145

A solution of 2-(4-heptyloxyphenyl)-5-(4-bromophenyl)thiazole (2.06 g) in dry tetrahydrofuran (60 ml) was cooled to  $-60^\circ\text{C}$ , and a solution of n-butyllithium (1.56M in n-hexane, 4.05 ml) was added slowly to maintain the reaction  
15 temperature at  $-60^\circ\text{C}$ . After stirring for 1 hour, dry-ice (4 g) was added. The reaction mixture was allowed to warm to room temperature over 30 minutes. To the reaction mixture was added water (20 ml) and 0.5N hydrochloric acid (80 ml), then extracted with dichloromethane (700 ml). The organic layer was washed  
20 with brine, and dried over magnesium sulfate. Magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure. The solids were slurried in acetonitrile and collected by filtration to give 4-[5-(4-heptyloxyphenyl)thiazol-2-yl]benzoic acid (1.68 g).

25 IR (KBr) : 2929.3, 2856.1, 2674.8, 2549.4, 1683.6,  
1604.5, 1432.9, 1297.9, 1253.5  $\text{cm}^{-1}$   
NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.70-1.00 (3H, m), 1.10-1.60 (8H, m),  
1.60-1.90 (2H, m), 4.04 (2H, t,  $J=6.4\text{Hz}$ ), 7.07 (2H,  
d,  $J=8.7\text{Hz}$ ), 7.83 (2H, d,  $J=8.2\text{Hz}$ ), 7.91 (2H, d,  
30  $J=8.7\text{Hz}$ ), 8.00 (2H, d,  $J=8.2\text{Hz}$ ), 8.39 (1H, s)

APCI-MS ( $m/z$ ) : 396

The following compound was obtained in a manner similar to that of Preparation 19.

Preparation 146

35 N-[4-[5-(4-Pentyloxyphenyl)-1,3,4-thiadiazol-2-

yl]benzoyl]-N'-(4-methoxycarbonylbenzoyl)hydrazine

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.91 (3H, t, J=6.9Hz), 1.28-1.52 (4H, m), 1.68-1.86 (2H, m), 3.91 (3H, s), 4.08 (2H, t, J=6.5Hz), 7.14 (2H, d, J=8.8Hz), 7.98 (2H, d, J=8.8Hz), 8.01-8.24 (8H, m), 10.82 (2H, s)

5

MASS (m/z) : 545 (M<sup>+</sup>+1)

#### Preparation 147

To a solution of 1-tert-butoxycarbonyl-4-(4-chlorophenyl)-4-methoxypiperidine (0.72 g) in ethyl acetate (10 ml) was added 4N HCl in ethyl acetate (5.5 ml). After stirring for 6.7 hours, the reaction mixture was poured into a mixture of ethyl acetate and water, followed by alkalification of the solution to pH 12. The organic layer was successively washed with water and brine and dried over magnesium sulfate. The solvent was evaporated in vacuo to give 4-(4-chlorophenyl)-4-methoxypiperidine (0.39 g).

10

15

IR (Film) : 2943, 2827, 1541 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.7-2.1 (4H, m), 2.17 (1H, s), 2.9-3.2 (7H, m), 7.33 (4H, s)

20

The following compound was obtained in a manner similar to that of Preparation 147.

#### Preparation 148

1-[4-(5-Methoxypentyloxy)biphenyl-4-yl]piperazine dihydrochloride

25

IR (KBr) : 2940.9, 2508.9, 1498.4, 1249.6 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.51-1.83 (6H, m), 3.34 (3H, s), 3.40 (2H, t, J=6.2Hz), 3.93 (2H, t, J=6.4Hz), 4.00-4.40 (8H, m), 6.84-6.89 (2H, m), 7.36-7.40 (2H, m), 7.58-7.62 (2H, m), 7.87-7.92 (2H, m), 9.90-10.15 (1H, m)

30

MASS (m/z) : 355 (M+1)

#### Preparation 149

To a solution of 4-hydroxyacetophenone (10 g) and pyridinium hydrobromide perbromide (23.5 g) in acetic acid (80

35



ml) was added hydrogenbromide (30% in acetic acid solution) (40 ml) and the mixture was stirred overnight at ambient temperature. The reaction mixture was added to ice water and extracted with ethyl acetate. The organic layer was taken and dried over magnesium sulfate. Magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to afford 2-bromo-1-(4-hydroxyphenyl)ethanone (1.72 g).

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 4.40 (2H, s), 5.78 (1H, s), 6.92 (2H, d, J=8.8Hz), 7.94 (2H, d, J=8.8Hz)

MASS (m/z) : 217 (M+H<sup>+</sup>)

The following compound was obtained in a manner similar to that of Preparation 149.

#### Preparation 150

2-Bromo-1-(4-pentyloxyphenyl)ethanone

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.94 (3H, t, J=6.8Hz), 1.3-1.5 (4H, m), 1.82 (2H, q, J=6.8Hz), 4.03 (2H, t, J=6.8Hz), 4.40 (2H, s), 6.94 (2H, d, J=9.0Hz), 7.96 (2H, d, J=9.0Hz)

MASS (m/z) : 287 (M+H<sup>+</sup>)

#### Preparation 151

A solution of 1-(4-aminophenyl)-1H-pyrazol-4-carboxylic acid methyl ester (3.0 g) in N,N-dimethylformamide (30 ml) was treated with potassium carbonate (5.72 g), sodium iodide (4.14 g) and 1,5-dibromopentane, and the mixture was stirred for 20 hours at room temperature and 6 hours at 80°C, during which period additional N,N-dimethylformamide (20 ml), 1,5-dibromopentane (1.14 g) and potassium carbonate (0.95 g) were added. The reaction mixture was cooled to room temperature and poured into water. The precipitate was collected by filtration, dried over under reduced pressure. The residue was purified by silica gel chromatography (dichloromethane elution) to give 1-(4-piperidylphenyl)-1H-pyrazol-4-carboxylic acid methyl ester (1.34 g).

IR (KBr) : 1720, 1521, 1248 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.5-1.8 (6H, m), 3.21 (4H, t, J=5.3Hz),

3.86 (3H, s), 6.98 (2H, d, J=9.1Hz), 7.53 (2H, d,

J=9.1Hz), 8.06 (1H, s), 8.29 (1H, s)

MASS (m/z) : 286 (M<sup>+</sup>+1)

The following compound was obtained in a manner similar to that of Preparation 151.

5 Preparation 152

1-(4-Pyrrolidinylphenyl)-1H-pyrazol-4-carboxylic acid methyl ester

IR (KBr) : 1720, 1541, 1525, 1246 cm<sup>-1</sup>

10 NMR (CDCl<sub>3</sub>, δ) : 2.0-2.1 (4H, m), 3.2-3.4 (4H, m), 3.86 (3H, s), 6.59 (2H, dd, J=6.9 and 2.1Hz), 7.49 (2H, dd, J=6.9 and 2.1Hz), 8.05 (1H, s), 8.25 (1H, s)

MASS (m/z) : 294 (M<sup>+</sup>+23)

Preparation 153

15 To a suspension of cyclohexane-1,4-dicarboxylic acid monomethyl ester (1.57 g) in thionyl chloride (3.14 ml) was added N,N-dimethylformamide (2 drops) and the mixture was stirred under refluxing for 1 hour. The reaction mixture was concentrated by evaporation under reduced pressure to give 4-chlorocarbonylcyclohexane carboxylic acid methyl ester  
20 (1.78 g).

NMR (CDCl<sub>3</sub>, δ) : 1.38-1.64 (4H, m), 2.09-2.32 (5H, m), 2.64-2.77 (1H, m), 3.68 (3H, s)

Preparation 154

25 Thionyl chloride (8.47 ml) was added dropwise to methanol (54 ml) at 10°C. To the solution was added trans-1,4-cyclohexane dicarboxylic acid (4 g) and the mixture was stirred for 24 hours at ambient temperature. The reaction mixture was evaporated under reduced pressure to give cyclohexane-1,4-dicarboxylic acid dimethyl ester (4.68 g).

30 IR (KBr) : 1729.8, 1195.6 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>, δ) : 1.34-2.15 (8H, m), 2.23-2.34 (2H, m), 3.67 (6H, s)

MASS (m/z) : 201 (M+1)

35 The following compounds [Preparations 155 to 157] were obtained in a manner similar to that of Preparation 154.

Preparation 155

2,5-Dimethyl-terephthalic acid dimethyl ester

IR (KBr) : 1722.1, 1261.2, 1101.2  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.57 (6H, s), 3.91 (6H, s), 7.76 (2H, s)

MASS (m/z) : 223 (M+1)

Preparation 156

2,4-Hexendioic acid dimethyl ester

IR (KBr) : 1702.8, 1612.2, 1249.6  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.71 (6H, s), 6.49 (2H, dd, J=3.1 and 11.5Hz), 7.40 (2H, dd, J=3.1 and 11.5Hz)

MASS (m/z) : 171 (M+1)

Preparation 157

Naphthalene-1,4-dicarboxylic acid dimethyl ester

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 4.03 (6H, s), 7.65 (2H, q, J=3.3Hz), 8.09 (2H, s), 8.83 (2H, q, J=3.3Hz)

MASS (m/z) : 245 (M+1)

The following compounds [Preparations 158 to 162] were obtained in a manner similar to that of Preparation 153.

Preparation 158

5-Chlorocarbonylthiophene-2-carboxylic acid methyl ester

IR (KBr) : 1724.0, 1666.2, 1251.6  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.86 (3H, s), 7.73-7.87 (2H, m)

Preparation 159

4-Chlorocarbonyl-2,5-dimethylbenzoic acid methyl ester

IR (KBr) : 1756.8, 1718.3, 1220.7  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.54 (3H, s), 2.60 (3H, s), 3.93 (3H, s), 7.78 (1H, s), 8.03 (1H, s)

Preparation 160

5-Chlorocarbonyl-2,4-pentenoic acid methyl ester

IR (KBr) : 1745.3, 1714.4, 1243.9  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.70 (3H, s), 6.29-6.64 (2H, m), 7.24-7.64 (2H, m)

Preparation 161

4-Chlorocarbonylnaphthalene-1-carboxylic acid methyl ester

IR (KBr) : 1762.6, 1724.0, 1257.4  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.98 (3H, s), 7.68-7.77 (2H, m), 8.14 (2H, s), 8.66-8.82 (2H, m)

Preparation 162

6-Chlorocarbonylnaphthalene-2-carboxylic acid methyl ester

10 IR (KBr) : 1743.3, 1714.4, 1290.1  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.94 (3H, s), 8.04-8.08 (2H, m), 8.21-8.27 (2H, m), 8.68-8.71 (2H, m)

Preparation 163

15 To a solution of 4-piperidin-1-yl-benzonitrile (3 g) and thiosemicarbazide (1.8 g) in toluene (30 ml) was added trifluoroacetic acid (20 ml) and the mixture was stirred at 60°C for 6 hours. The reaction mixture was placed in water, the solution was adjusted to pH 9 with 1N sodium hydroxide and the precipitate was collected by filtration to give 5-(4-piperidin-1-yl-phenyl)-[1,3,4]thiadiazol-2-yl-amine (3.58 g).

IR (KBr) : 2933, 2838, 1604, 1502, 1463, 1386, 1349 1245, 1126, 1043, 821  $\text{cm}^{-1}$

25 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.57 (6H, m), 3.24 (4H, m), 6.96 (2H, d,  $J=8.8\text{Hz}$ ), 7.19 (2H, s), 7.54 (2H, d,  $J=8.8\text{Hz}$ )

MASS ( $m/z$ ) : 261 ( $M+H^+$ )

The following compounds [Preparations 164 to 169] were obtained in a manner similar to that of Preparation 163.

Preparation 164

30 5-(4-Morpholinylphenyl)-[1,3,4]thiadiazol-2-yl-amine

IR (KBr) : 3274, 3106, 1604, 1508, 1465, 1378, 1324, 1267, 1238, 1122  $\text{cm}^{-1}$

35 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 3.19 (4H, t,  $J=4.8\text{Hz}$ ), 3.74 (4H, t,  $J=4.8\text{Hz}$ ), 7.00 (2H, d,  $J=8.8\text{Hz}$ ), 7.22 (2H, s), 7.59 (2H, d,  $J=8.8\text{Hz}$ )

MASS (m/z) : 263 (M+H<sup>+</sup>)

Preparation 165

5-[4-(cis-2,6-Dimethylmorpholin-4-yl)phenyl]-  
[1,3,4]thiadiazol-2-yl-amine

5 IR (KBr) : 3272, 3106, 1608, 1525, 1469, 1376, 1346, 1245,  
1176, 1145, 1081 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.16 (6H, d, J=6.2Hz), 2.31 (2H, t,  
J=11.5Hz), 3.6-3.8 (4H, m), 7.00 (2H, d, J=8.8Hz),  
7.21 (2H, s), 7.58 (2H, d, J=8.8Hz)

10 MASS (m/z) : 291 (M+H<sup>+</sup>)

Preparation 166

5-(4-Thiomorpholinophenyl)-[1,3,4]thiadiazol-2-yl-  
amine

15 IR (KBr) : 3340, 3270, 3129, 1604, 1506, 1467, 1384, 1295,  
1230, 1195 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 2.64 (4H, t, J=5.0Hz), 3.66 (4H, t,  
J=5.0Hz), 6.97 (2H, d, J=8.8Hz), 7.21 (2H, s), 7.57  
(2H, d, J=8.8Hz),

MASS (m/z) : 279 (M+H<sup>+</sup>)

20 Preparation 167

5-[4-(4-Ethylpiperazinyphenyl)]-[1,3,4]thiadiazol-2-  
yl-amine

IR (KBr) : 3278, 3120, 2967, 2829, 1685, 1608, 1517, 1467,  
1388, 1240, 1203, 1130 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 1.04 (3H, t, J=7.2Hz), 2.41 (2H, q,  
J=7.2Hz), 2.51 (4H, m), 3.23 (4H, m), 6.99 (2H, d,  
J=8.8Hz), 7.21 (2H, s), 7.57 (2H, d, J=8.8Hz)

MASS (m/z) : 290 (M+H<sup>+</sup>)

Preparation 168

30 5-[4-(4-Cyclohexylpiperazinyphenyl)]-  
[1,3,4]thiadiazol-2-yl-amine

IR (KBr) : 3016, 2950, 2865, 1743, 1672, 1606, 1513, 1456,  
1430, 1402, 1201, 1133 cm<sup>-1</sup>

35 NMR (DMSO-d<sub>6</sub>, δ) : 1.0-1.6 (5H, m), 1.63 (1H, d, J=10Hz),  
1.85 (2H, d, J=10Hz), 2.09 (2H, d, J=10Hz), 2.8-

3.3 (5H, m), 3.55 (2H, m), 3.99 (2H, d, J=10Hz), 7.09  
(2H, d, J=8.8Hz), 7.65 (2H, d, J=8.8Hz)

MASS (m/z) : 344 (M+H<sup>+</sup>)

#### Preparation 169

5           4-(5-Amino-[1,3,4]thiadiazol-2-yl)benzoic acid methyl  
ester trifluoroacetic acid salt

IR (KBr) : 3004, 2746, 1726, 1675, 1645, 1608, 1436, 1284,  
1211, 1186, 1137, 1112 cm<sup>-1</sup>

10           NMR (DMSO-d<sub>6</sub>, δ) : 3.88 (3H, s), 7.19 (2H, s), 7.90 (2H,  
d, J=8.5Hz), 8.04 (2H, d, J=8.5Hz)

MASS (m/z) : 236 (M+H<sup>+</sup>)

#### Preparation 170

To a mixture of 4-methoxycarbonylphenylboronic acid  
(2.01 g) and 1-bromo-4-ethoxymethylbenzene (2.00 g) in a mixed  
15 solvent of ethylene glycol dimethyl ether (20 ml) and 2M aqueous  
sodium carbonate solution (6 ml) was added  
tetrakis(triphenylphosphine)palladium (0) (0.54 g). The  
mixture was heated at 80°C for 5 hours. After cooling to room  
temperature, water (150 ml) was added to the reaction mixture  
20 and the resulting precipitate was collected by filtration,  
washed thoroughly with water and dried to give a crude solid.  
This solid was purified by column chromatography on silica gel  
(60 g) eluting successively with the following solvents:  
(1)n-hexane : ethyl acetate=50:1, (2) n-hexane : ethyl  
25 acetate=10:1. The fractions containing the object compound  
were concentrated and dried to give methyl 4-(4'-  
ethoxymethylphenyl)benzoate as a white solid (1.85 g).

30           NMR (CDCl<sub>3</sub>, δ) : 1.27 (3H, t, J=7.0Hz), 3.58 (2H, q,  
J=7.0Hz), 3.94 (3H, m), 4.56 (2H, s), 7.44 (2H, d,  
J=8.7Hz), 7.54-7.61 (4H, m), 8.04-8.15 (2H, m)

The following compound was obtained in a manner similar  
to that of Preparation 170.

#### Preparation 171

35           Methyl 4-[4'-(2-methoxyethoxymethyl)phenyl]benzoate  
NMR (CDCl<sub>3</sub>, δ) : 3.41 (3H, m), 3.55-3.70 (4H, m), 3.94

(3H, s), 4.63 (2H, s), 7.45 (2H, d, J=8.3Hz),  
7.56-7.74 (4H, m), 8.07-8.20 (2H, m)

MASS (m/z) : 301 (M<sup>+</sup>+1)

#### Preparation 172

5 To an ice-cooled solution of 4-bromobenzyl bromide (3.00 g) and 2-methoxyethanol (1.04 ml) in tetrahydrofuran (30 ml) was added sodium hydride (60%) (0.58 g) in a stream of nitrogen. The mixture was stirred at this temperature for 15 minutes and at room temperature for further 4 hours. To the mixture was  
10 added water (1 ml) under ice-cooling. The reaction mixture was diluted with ethyl acetate and washed successively with water and saturated sodium chloride solution. The organic layer was dried over magnesium sulfate, filtered and evaporated to give 1-bromo-4-(2-methoxyethoxymethyl)benzene  
15 (3.10 g) as a pale yellow oil.

NMR (DMSO-d<sub>6</sub>, δ) : 3.25 (3H, m), 3.43-3.60 (2H, m), 4.46 (2H, s), 7.28 (2H, d, J=8.5Hz), 7.49-7.60 (4H, m)

The following compounds [Preparations 173 to 175] were obtained in a manner similar to that of Preparation 172.

#### 20 Preparation 173

Ethyl 4-(4-propoxypiperidin-1-yl)benzoate

NMR (DMSO-d<sub>6</sub>, δ) : 0.87 (3H, t, J=7.4Hz), 1.28 (3H, t, J=7.1Hz), 1.36-1.60 (4H, m), 1.80-1.98 (2H, m), 3.00-3.20 (2H, m), 3.39 (2H, t, J=6.5Hz), 3.41-3.76  
25 (3H, m), 4.23 (2H, q, J=7.1Hz), 6.97 (2H, d, J=9.1Hz), 7.76 (2H, d, J=9.0Hz)

MASS (m/z) : 292 (M<sup>+</sup>+1)

#### Preparation 174

Ethyl 4-(4-benzyloxypiperidin-1-yl)benzoate

30 NMR (DMSO-d<sub>6</sub>, δ) : 1.28 (3H, t, J=7.1Hz), 1.45-1.66 (2H, m), 1.85-2.02 (2H, m), 3.00-3.21 (2H, m), 3.55-3.78 (3H, m), 4.23 (2H, q, J=7.1Hz), 4.55 (2H, s), 6.98 (2H, d, J=9.1Hz), 7.23-7.43 (5H, m), 7.76 (2H, d, J=9.0Hz)

35 MASS (m/z) : 340 (M<sup>+</sup>+1)

Preparation 175

1-(4-Heptyloxyethylphenyl)-1H-pyrazol-4-carboxylic acid methyl ester

IR (KBr) : 1703, 1558, 1265  $\text{cm}^{-1}$

5 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.85 (3H, m), 1.1-1.6 (10H, m), 3.44 (2H, t,  $J=6.4\text{Hz}$ ), 3.81 (3H, s), 4.49 (2H, s), 7.45 (2H, d,  $J=8.5\text{Hz}$ ), 7.91 (2H, d,  $J=8.5\text{Hz}$ ), 8.15 (1H, s), 9.11 (1H, s)

MASS ( $m/z$ ) : 331 ( $M^+ + 1$ )

10 Preparation 176

To a solution of methyl 4-(4-hydroxyphenyl)benzoate (3.00 g) and cyclohexanol (1.58 g) in tetrahydrofuran (60 ml) was added dropwise diethyl azodicarboxylate (2.48 ml) at 0-10°C under nitrogen atmosphere, and the mixture was stirred at ambient temperature for 4 hours. After concentration, to the residue was added ethyl acetate (50 ml) and n-hexane (10 ml), and the resulting precipitate was removed by filtration and discarded. To the filtrate was added silica gel (12 g) and the mixture was evaporated. The residue was purified by column chromatography on silica gel (80 g) eluting with a mixed solvent of 5% ethyl acetate in n-hexane to give methyl 4-(4-cyclohexyloxyphenyl)benzoate (1.79 g) as a white solid.

IR (KBr) : 1720, 1603, 1525, 1495, 1437  $\text{cm}^{-1}$

25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.22-1.66 (6H, m), 1.72-1.90 (2H, m), 1.95-2.10 (2H, m), 3.93 (3H, s), 4.22-4.37 (1H, m), 6.89-7.03 (2H, m), 7.47-7.76 (4H, m), 8.00-8.13 (2H, m)

MASS ( $m/z$ ) : 311 ( $M^+ + 1$ )

30 The following compound was obtained in a manner similar to that of Preparation 176.

Preparation 177

4-Cyclohexyloxybenzoic acid methyl ester

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.20-2.10 (10H, m), 3.88 (3H, s), 4.20-4.40 (1H, m), 6.85-6.95 (2H, m), 7.90-8.00 (2H, m)



APCI MASS (positive) : 235.2 ( $M^+ + 1$ )

Preparation 178

To an ice-cooled solution of ethyl 4-(piperazin-1-yl)benzoate (2.00 g) and 4-methylcyclohexanone (1.05 ml) in a mixed solvent of methanol (40 ml) and acetic acid (1.47 ml) was added sodium cyanoborohydride (0.59 g) in a stream of nitrogen. The mixture was stirred at this temperature for 1 hour and at room temperature for 17 hours. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate solution and the resulting precipitate was collected by filtration, washed thoroughly with water and dried to give a mixture of cis and trans products. This mixture was separated by column chromatography on silica gel eluting with a mixed solvent of methylene chloride-methanol (from 0% to 2% gradient solution) to give ethyl 4-[4-(cis-4-methylcyclohexyl)piperazin-1-yl]benzoate (0.80 g) as a pale green solid and ethyl 4-[4-(trans-4-methylcyclohexyl)piperazin-1-yl]benzoate (0.64 g) as a pale green solid. Trans-product was confirmed by X-ray crystal analysis.

Ethyl 4-[4-(cis-4-methylcyclohexyl)piperazin-1-yl]benzoate

IR (KBr) : 1697, 1608, 1520, 1446  $\text{cm}^{-1}$

NMR (DMSO- $D_6$ ,  $\delta$ ) : 0.89 (3H, d,  $J=6.8\text{Hz}$ ), 1.28 (3H, t,  $J=7.1\text{Hz}$ ), 1.23-1.52 (6H, m), 1.52-1.76 (3H, m), 2.07-2.25 (1H, m), 2.47-2.63 (4H, m), 3.20-3.40 (4H, m), 4.23 (2H, q,  $J=7.1\text{Hz}$ ), 6.96 (2H, d,  $J=9.1\text{Hz}$ ), 7.78 (2H, d,  $J=8.9\text{Hz}$ )

MASS (m/z) : 331 ( $M^+ + 1$ )

Ethyl 4-[4-(trans-4-methylcyclohexyl)piperazin-1-yl]benzoate

IR (KBr) : 1709, 1608, 1518, 1444  $\text{cm}^{-1}$

NMR (DMSO- $D_6$ ,  $\delta$ ) : 0.85 (3H, d,  $J=6.8\text{Hz}$ ), 0.80-1.02 (2H, m), 1.28 (3H, t,  $J=7.1\text{Hz}$ ), 1.09-1.56 (3H, m), 1.56-1.88 (4H, m), 2.08-2.34 (1H, m), 2.50-2.67 (4H,

m), 3.18-3.34 (4H, m), 4.23 (2H, q, J=7.1Hz), 6.95 (2H, d, J=9.1Hz), 7.77 (2H, d, J=8.9Hz)

MASS (m/z) : 331 (M<sup>+</sup>+1)

5 The following compound was obtained in a manner similar to that of Preparation 178.

Preparation 179

Ethyl 4-[4-(4,4-dimethylcyclohexyl)piperazin-1-yl]benzoate

10 NMR (CDCl<sub>3</sub>, δ) : 0.91 (6H, s), 1.07-1.55 (6H, m), 1.36 (3H, t, J=7.1Hz), 1.64-1.82 (2H, m), 2.10-2.30 (1H, m), 2.72 (4H, t, J=5.1Hz), 3.33 (4H, t, J=5.1Hz), 4.32 (2H, q, J=7.1Hz), 6.86 (2H, d, J=9.1Hz), 7.87-7.99 (2H, m)

MASS (m/z) : 345 (M<sup>+</sup>+1)

15 Preparation 180

To a mixture of cesium carbonate (1.90 g), palladium (II) acetate (46.7 mg) and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (194 mg) in toluene (3.3 ml) was successively added a solution of cis-2,6-dimethyl morpholine (0.58 g) in toluene  
20 (5 ml) and methyl 4-(4-trifluoromethanesulfonyloxyphenyl)-benzoate (1.50 g) in a stream of nitrogen. The mixture was stirred at ambient temperature for 30 minutes and refluxed for further 6 hours. After cooling to room temperature, water was added to the reaction mixture and the mixture was extracted  
25 with methylene chloride. The organic layer was washed with saturated aqueous sodium chloride solution, dried over magnesium sulfate, filtered and concentrated in vacuo. The residue was pulverized with acetonitrile and collected by filtration to give methyl 4-[4-(cis-2,6-dimethylmorpholino-  
30 phenyl)]benzoate (525 mg) as a pale yellow solid.

IR (KBr) : 1720, 1603, 1497, 1446 cm<sup>-1</sup>

35 NMR (CDCl<sub>3</sub>, δ) : 1.28 (6H, d, J=6.3Hz), 2.46 (1H, d, J=10.6Hz), 2.49 (1H, d, J=10.6Hz), 3.46-3.62 (2H, m), 3.72-3.94 (2H, m), 3.93 (3H, s), 6.98 (2H, d, J=8.9Hz), 7.51-7.70 (4H, m), 8.02-8.14 (2H, m)

MASS (m/z) : 326 ( $M^+ + 1$ )

The following compound was obtained in a manner similar to that of Preparation 180.

Preparation 181

5 Methyl 4-[4-(4-cyclohexylpiperazin-1-yl)phenyl]benzoate

IR (KBr) : 2929, 2852, 2829, 1714, 1603, 1529, 1498,  
1439  $\text{cm}^{-1}$

10 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00-1.41 (5H, m), 1.51-2.05 (5H, m),  
2.24-2.43 (1H, m), 2.69-2.84 (4H, m), 3.22-3.36 (4H, m), 3.93 (3H, s), 7.00 (2H, d,  $J=8.9\text{Hz}$ ), 7.48-7.68 (4H, m), 8.00-8.12 (2H, m)

MASS (m/z) : 379 ( $M^+ + 1$ )

Preparation 182

15 To a suspension of 2-amino-5-(4-methoxyphenyl)-1,3,4-thiadiazole (7.2 g) in ethanol (50 ml) was added ethyl 4-bromoacetylbenzoate (11.3 g) and the mixture was stirred under refluxing for 2.5 hours. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by  
20 filtration and dried. To a suspension of the powder in xylene (50 ml) was added trifluoroacetic acid (5 ml) and the mixture was stirred under refluxing for 3.5 hours. The reaction mixture was pulverized with diisopropyl ether. The precipitate was collected by filtration and dried to give  
25 4-[2-(4-methoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester trifluoroacetic acid salt (13.7 g).

IR (KBr) : 2360.4, 1746.3, 1604.5, 1483.0  $\text{cm}^{-1}$

MASS (m/z) : 380 ( $(M-\text{TFA}) + \text{H}^+$ )

30 The following compounds [Preparations 183 to 190] were obtained in a manner similar to that of Preparation 182.

Preparation 183

4-[2-(4-Piperidin-1-yl-phenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester  
35 trifluoroacetic acid salt

IR (KBr) : 2940, 2584, 2474, 1702, 1608, 1523, 1471, 1409,  
1367, 1280  $\text{cm}^{-1}$

MASS (m/z) : 433 ((M-TFA)+H<sup>+</sup>)

Preparation 184

5        4-[2-(4-Morpholin-4-yl-phenyl)imidazo[2,1-  
b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester  
trifluoroacetic acid salt

IR (KBr) : 2669, 1706, 1606, 1473, 1274, 1236, 1176, 1118,  
1020, 929  $\text{cm}^{-1}$

10       MASS (m/z) : 435 ((M-TFA)+H<sup>+</sup>)

Preparation 185

4-[2-(cis-2,6-Dimethylmorpholin-4-yl-  
phenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid  
ethyl ester trifluoroacetic acid salt

15       IR (KBr) : 2979, 1710, 1606, 1473, 1371, 1278, 1241, 1176,  
1106  $\text{cm}^{-1}$

MASS (m/z) : 463 ((M-TFA)+H<sup>+</sup>)

Preparation 186

20       4-[2-(4-Thiomorpholin-4-yl-phenyl)imidazo[2,1-  
b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester  
trifluoroacetic acid salt

IR (KBr) : 2979, 1708, 1604, 1504, 1471, 1274,  
1193, 1105  $\text{cm}^{-1}$

MASS (m/z) : 451 ((M-TFA)+H<sup>+</sup>)

25       Preparation 187

4-[2-[4-(4-Ethylpiperazin-1-yl)phenyl]imidazo[2,1-  
b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester  
trifluoroacetic acid salt

30       IR (KBr) : 2983, 2931, 2674, 2605, 1702, 1606, 1471,  
1405, 1282, 1241, 1201  $\text{cm}^{-1}$

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.23-1.38 (6H, m), 3.30-3.23 (6H, m),  
3.61 (2H, d, J=8.2Hz), 4.12 (2H, d, J=8.2Hz), 4.33  
(2H, q, J=7.2Hz), 7.20 (2H, d, J=8.8Hz), 7.85 (2H,  
d, J=8.8Hz), 8.02 (4H, s), 8.86 (1H, s)

35       MASS (m/z) : 462 ((M-TFA)+H<sup>+</sup>)

Preparation 188

4-[2-[4-(4-Cyclohexylpiperazin-1-yl)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester trifluoroacetic acid salt

5 IR (KBr) : 2935, 2586, 1708, 1604, 1571, 1488, 1409,  
1367, 1278, 1199, 1106  $\text{cm}^{-1}$   
MASS (m/z) : 516 ((M-TFA)+H<sup>+</sup>)

Preparation 189

10 4-[6-(4-Hydroxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-2-yl]benzoic acid methyl ester trifluoroacetic acid salt

IR (KBr) : 3214, 3027, 1720, 1629, 1610, 1513, 1434, 1284,  
1187, 1112  $\text{cm}^{-1}$   
NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 3.91 (3H, s), 7.72 (2H, d, J=8.5Hz),  
15 7.91 (2H, d, J=8.5Hz), 8.12 (4H, s), 8.61 (1H, s)  
MASS (m/z) : 352 ((M-TFA)+H<sup>+</sup>)

Preparation 190

20 4-[6-(4-Pentyloxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-2-yl]benzoic acid methyl ester trifluoroacetic acid salt

IR (KBr) : 2952, 2869, 1720, 1612, 1494, 1471, 1436, 1405,  
1280, 1251, 1182, 1110  $\text{cm}^{-1}$   
MASS (m/z) : 422 ((M-TFA)+H<sup>+</sup>)

Preparation 191

25 A solution of methyl 4-[4-(4-bromobutoxy)phenyl]benzoate (1.40 g) in methanol (14 ml) was treated with 28% sodium methoxide in methanol (14 ml) and the solution was refluxed for 5 hours. After cooling to room temperature, the reaction mixture was poured into cold 1N-  
30 hydrochloric acid (110 ml) and the resulting precipitate was collected by filtration, washed thoroughly with water and dried to give a white solid. To a mixture of this solid in methanol (20 ml) was added concentrated sulfuric acid (0.5 ml) and refluxed for 4 hours. After cooling to room temperature,  
35 the reaction mixture was poured into cold water and the

resulting precipitate was collected by filtration, washed thoroughly with water and dried to give methyl 4-[4-(4-methoxybutoxy)phenyl]benzoate (1.16 g) as a white solid.

IR (KBr) : 2949, 2873, 1720, 1603, 1529, 1498, 1439  $\text{cm}^{-1}$

5 NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.54-1.85 (4H, m), 3.24 (3H, s), 3.38 (2H, t,  $J=6.2\text{Hz}$ ), 3.87 (3H, s), 4.04 (2H, t,  $J=6.1\text{Hz}$ ), 7.05 (2H, t,  $J=8.8\text{Hz}$ ), 7.69 (2H, d,  $J=8.7\text{Hz}$ ), 7.78 (2H, d,  $J=8.4\text{Hz}$ ), 8.00 (2H, d,  $J=8.4\text{Hz}$ )

MASS ( $m/z$ ) : 315 ( $M^+ + 1$ )

10 The following compounds [Preparations 192 to 194] were obtained in a manner similar to that of Preparation 191.

Preparation 192

Methyl 4-[4'-(3-methoxypropoxy)phenyl]benzoate

IR (KBr) : 2953, 2875, 1724, 1603, 1529, 1495, 1435  $\text{cm}^{-1}$

15 NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.96 (2H, m), 3.26 (3H, s), 3.49 (2H, t,  $J=6.3\text{Hz}$ ), 3.87 (3H, s), 4.08 (2H, t,  $J=6.4\text{Hz}$ ), 6.98-7.14 (2H, m), 7.64-7.86 (4H, m), 7.96-8.10 (2H, m)

MASS ( $m/z$ ) : 301 ( $M^+ + 1$ )

20 Preparation 193

1-Bromo-4-ethoxymethylbenzene

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.15 (3H, t,  $J=7.0\text{Hz}$ ), 3.47 (2H, q,  $J=7.0\text{Hz}$ ), 4.42 (2H, s), 7.28 (2H, d,  $J=8.5\text{Hz}$ ), 7.46-7.61 (2H, m)

25 Preparation 194

Methyl 4-[4-(3-ethoxypropoxy)phenyl]benzoate

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.11 (3H, t,  $J=7.0\text{Hz}$ ), 1.96 (2H, m), 3.43 (2H, q,  $J=7.0\text{Hz}$ ), 3.52 (2H, t,  $J=6.3\text{Hz}$ ), 3.87 (3H, s), 4.08 (2H, t,  $J=6.3\text{Hz}$ ), 7.06 (2H, d,  $J=8.8\text{Hz}$ ), 7.70 (2H, d,  $J=8.8\text{Hz}$ ), 7.78 (2H, d,  $J=8.5\text{Hz}$ ), 8.00 (2H, d,  $J=8.5\text{Hz}$ )

30

MASS ( $m/z$ ) : 315 ( $M^+ + 1$ )

Preparation 195

To a suspension of 4-[2-(4-hydroxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester (500 mg)

35

and potassium carbonate (2 g) in N,N-dimethylformamide (25 ml) was added 1,4-dibromobutane (1 ml) and the mixture was stirred at room temperature for 22 hours. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration and dried. To a suspension of the powder in N,N-dimethylformamide (25 ml) was added piperidine (2 ml) and the mixture was stirred at room temperature for 21 hours. The reaction mixture was pulverized with water. The precipitate was collected by filtration, washed with water, acetonitrile and diisopropyl ether and dried to give 4-[2-[4-(4-piperidin-1-yl-butyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester (479 mg).

IR (KBr) : 2933.2, 1708.6, 1608.3, 1471.4, 1274.7, 1176.4, 1101.2  $\text{cm}^{-1}$

MASS (m/z) : 505 ( $\text{M}+\text{H}^+$ )

The following compounds [Preparations 196 to 201] were obtained in a manner similar to that of Preparation 195.

Preparation 196

4-[2-[4-(5-Piperidin-1-yl-pentyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester

IR (KBr) : 2935, 1708, 1608, 1471, 1274, 1176, 1101  $\text{cm}^{-1}$

MASS (m/z) : 519 ( $\text{M}+\text{H}^+$ )

Preparation 197

4-[2-[4-(6-Piperidin-1-yl-hexyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester

IR (KBr) : 2933, 1710, 1608, 1471, 1274, 1176, 1103  $\text{cm}^{-1}$

MASS (m/z) : 533 ( $\text{M}+\text{H}^+$ )

Preparation 198

4-[2-[4-(5-Morpholin-4-yl-pentyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester

IR (KBr) : 2940, 1708, 1608, 1471, 1276, 1176

1116  $\text{cm}^{-1}$

MASS (m/z) : 521 (M+H<sup>+</sup>)

Preparation 199

4-[2-[4-[5-(cis-2,6-Dimethylmorpholin-4-yl)pentyloxy]phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester

IR (KBr) : 2937, 1708, 1608, 1471, 1409, 1369, 1307, 1278, 1176 cm<sup>-1</sup>

MASS (m/z) : 549 (M+H<sup>+</sup>)

Preparation 200

4-[2-[4-[6-(cis-2,6-Dimethylmorpholin-4-yl)hexyloxy]phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester

IR (KBr) : 2937, 1710, 1606, 1544, 1471, 1403, 1305, 1270, 1257, 1176 cm<sup>-1</sup>

MASS (m/z) : 563 (M+H<sup>+</sup>)

Preparation 201

4-[2-[4-(5-Thiomorpholin-4-yl-pentyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester

IR (KBr) : 2939, 1706, 1608, 1471, 1274, 1176, 1108 cm<sup>-1</sup>

MASS (m/z) : 537 (M+H<sup>+</sup>)

Preparation 202

To a suspension of 4-[2-(4-hydroxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester (1 g) and potassium carbonate (4 g) in N,N-dimethylformamide (50 ml) was added 1,5-dibromopentane (2 ml) and the mixture was stirred at room temperature for 6 hours. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, washed with water and methanol. To a suspension of the powder in methanol (10 ml) was added sodium methylate (28% in methanol) (20 ml) and the mixture was stirred at 80°C for 19 hours. The reaction mixture was pulverized with water. The precipitate was collected by filtration, washed with water, methanol and diisopropyl ether and dried to give 4-[2-[4-(5-methoxypentyloxy)phenyl]imidazo[2,1-



b][1,3,4]thiadiazol-6-yl]benzoic acid methyl ester (479 mg).

MASS (m/z) : 452 (M+H<sup>+</sup>)

The following compounds [Preparations 203 to 205] were obtained in a manner similar to that of Preparation 202.

5     Preparation 203

4-[2-[4-(6-Methoxyhexyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid methyl ester

IR (KBr) : 2935, 2861, 1712, 1608, 1591, 1533, 1471, 1417, 1305, 1259, 1178, 1116 cm<sup>-1</sup>

10     MASS (m/z) : 466 (M+H<sup>+</sup>)

Preparation 204

4-[2-[4-(7-Methoxyheptyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid methyl ester

IR (KBr) : 2933, 2858, 1714, 1608, 1591, 1533, 1469, 1419, 1305, 1259, 1178, 1112 cm<sup>-1</sup>

15     MASS (m/z) : 480 (M+H<sup>+</sup>)

Preparation 205

4-[2-[4-(8-Methoxyoctyloxy)phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid methyl ester

20     IR (KBr) : 2931, 2856, 1712, 1610, 1591, 1533, 1471, 1419, 1305, 1259, 1178, 1112 cm<sup>-1</sup>

MASS (m/z) : 494 (M+H<sup>+</sup>)

Preparation 206

25     A mixture of piperazin-1-carboxylic acid tert-butyl ester (0.64 g), 4-bromo-4'-(5-methoxypentyloxy)biphenyl (1 g), tris(dibenzylideneacetone)(chloroform)dipalladium(0) (59 mg), (S)-(-)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (0.12 g) and sodium tert-butoxide (0.55 g) in toluene (10 ml) was stirred for 54 hours at 90°C. The reaction  
30     mixture was added to a mixture of water and ethyl acetate. The organic layer was taken and dried over magnesium sulfate. The magnesium sulfate was filtered off, and the filtrate was evaporated under reduced pressure to give 4-[4'-(5-methoxypentyloxy)biphenyl-4-yl]piperazin-1-carboxylic  
35     acid tert-butyl ester (1.19 g).

IR (KBr) : 1691.3, 1504.2, 1232.3  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.49 (9H, s), 1.49-1.90 (6H, m), 3.14-3.19  
(4H, m), 3.34 (3H, s), 3.41 (2H, t,  $J=6.2\text{Hz}$ ),  
3.57-3.62 (4H, m), 3.99 (2H, t,  $J=6.4\text{Hz}$ ), 6.91-6.99  
5 (4H, m), 7.44-7.49 (4H, m)

MASS (m/z) : 455 (M+1)

The following compound was obtained in a manner similar  
to that of Preparation 206.

Preparation 207

10 4-[4-[4-(7-Methoxyheptylthio)phenyl]piperazin-1-  
yl]benzoic acid

IR (KBr) : 1681.6, 1585.2, 1423.2, 1230.4  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.20-1.55 (10H, m), 2.80 (2H, t,  
 $J=6.7\text{Hz}$ ), 3.20 (3H, s), 3.24-3.43 (10H, m),  
15 6.82-6.86 (2H, m), 6.94-6.98 (2H, m), 7.23-7.27 (2H,  
m), 7.69-7.73 (2H, m)

MASS (m/z) : 443.2 (M+1)

Preparation 208

1-tert-Butoxycarbonyl-4-[4-(4-  
20 cyclohexylphenyl)piperazin-1-yl]piperidine (3.3 g) and  
trifluoroacetic acid (10 ml) were mixed and the mixture was  
stirred at ambient temperature for 1 hour. The solution was  
placed in water, adjusted to pH 8 with 1N sodium hydroxide  
and extracted with ethyl acetate. The organic layer was  
25 separated, washed with brine, dried over magnesium sulfate  
and evaporated under reduced pressure to give 1-(4-  
cyclohexylphenyl)-4-piperidylpiperazine (3.83 g).

Preparation 209

To a suspension of 4-[2-(4-hydroxyphenyl)imidazo[2,1-  
30 b][1,3,4]thiadiazol-6-yl]benzoic acid (4.0 g) in ethanol (50  
ml) was added sulfuric acid (1.0 ml) and the mixture was  
stirred at 80°C for 9 hours. The reaction mixture was  
pulverized with water. The precipitate was collected by  
filtration, washed with water, acetonitrile and diisopropyl  
35 ether and dried to give 4-[2-(4-

hydroxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid ethyl ester (2.09 g).

IR (KBr) : 3215, 1679.7, 1608.3, 1473.3, 1288.2  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.34 (3H, t,  $J=7.1\text{Hz}$ ), 4.32 (2H, q,

5

$J=7.1\text{Hz}$ ), 6.96 (2H, d,  $J=8.5\text{Hz}$ ), 7.89 (2H, d,

$J=8.5\text{Hz}$ ), 8.02 (4H, s), 8.84 (1H, s), 10.40 (1H, s)

MASS (m/z) : 366 ( $M+H^+$ )

The following compound was obtained in a manner similar to that of Preparation 209.

10

Preparation 210

4-Cyclohexylbenzoic acid methyl ester

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.10-1.55 (5H, m), 1.65-1.95 (5H, m),

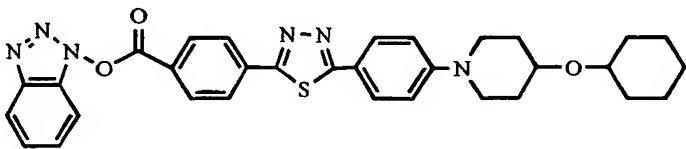
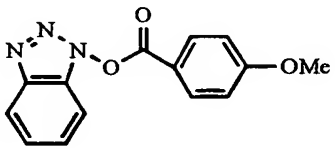
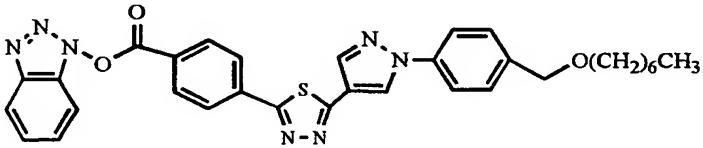
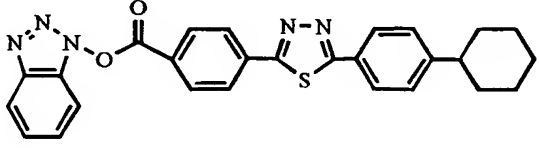
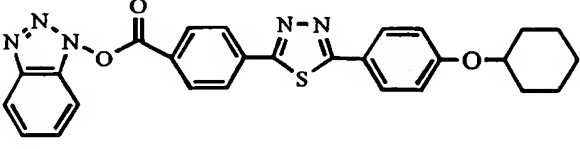
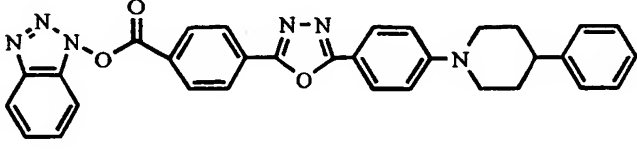
2.45-2.65 (1H, m), 3.89 (3H, s), 7.26 (2H, d,

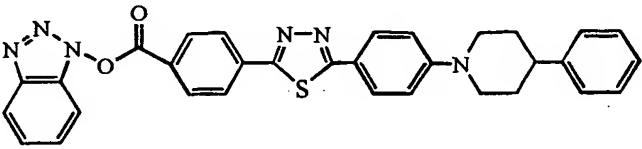
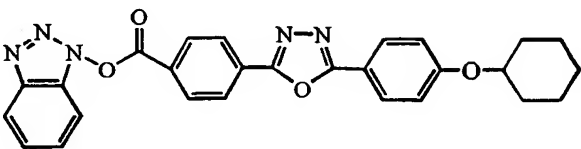
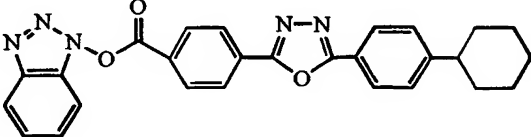
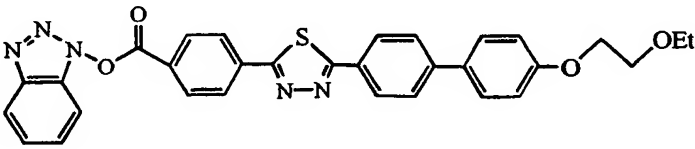
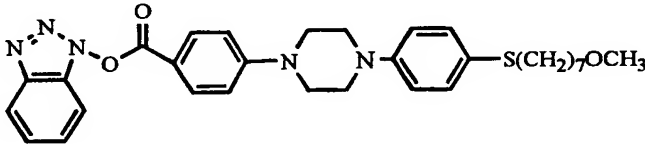
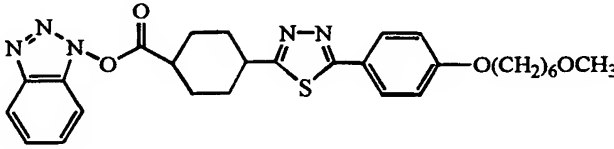
$J=8.2\text{Hz}$ ), 7.95 (2H, d,  $J=8.2\text{Hz}$ )

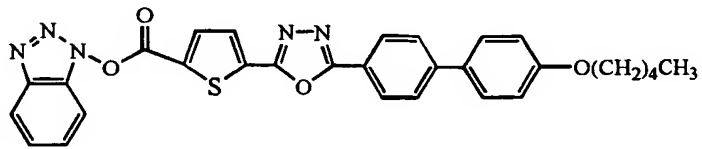
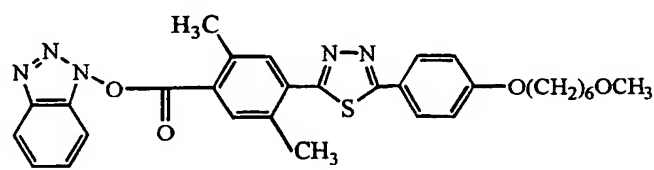
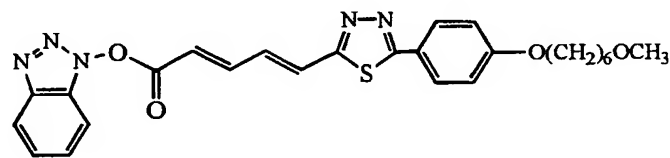
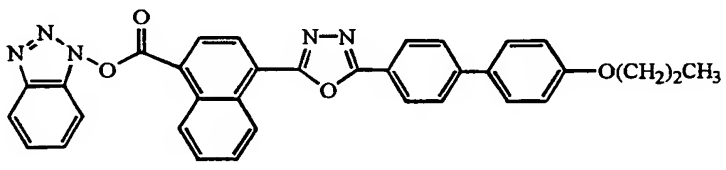
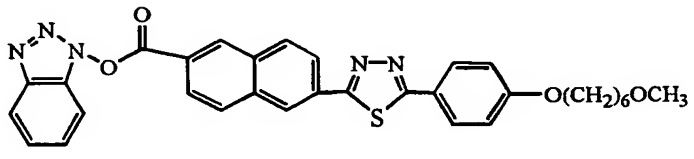
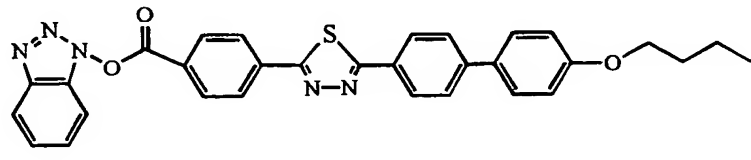
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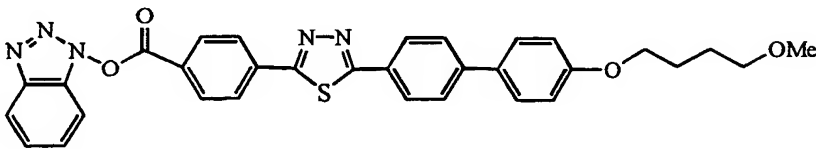
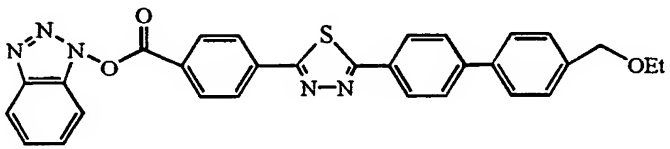
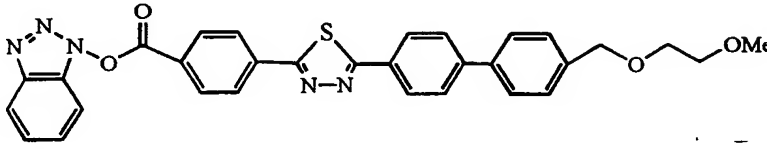
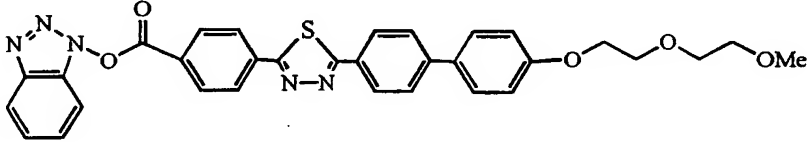
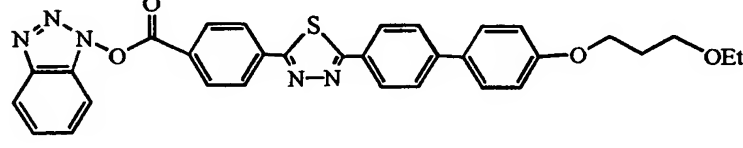
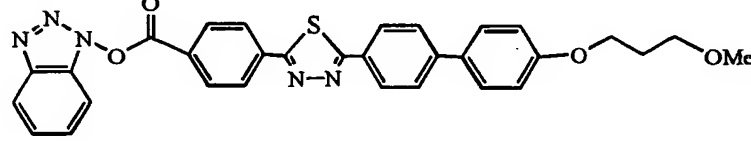
APCI MASS: 219 ( $M^++1$ )

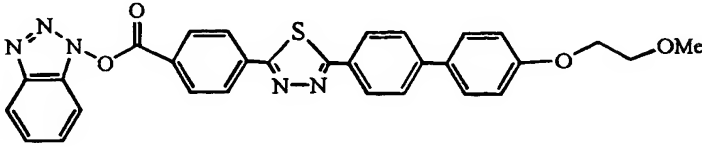
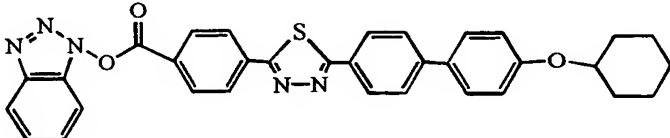
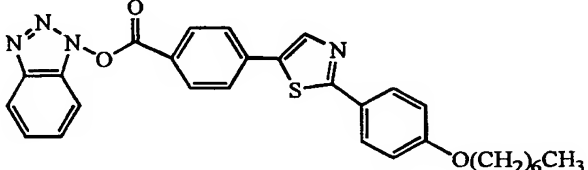
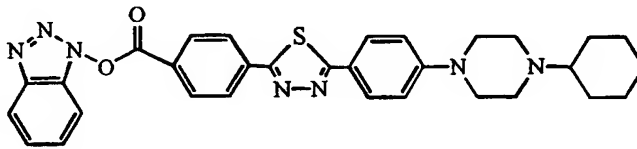
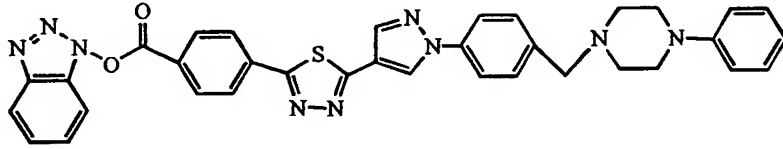
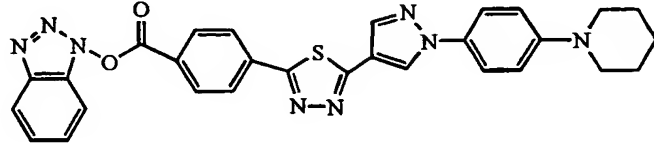
The Object Compounds (211) to (457) obtained in the following Preparations 211 to 457 are given in the tables as below.

Preparation No.	Formula
211	
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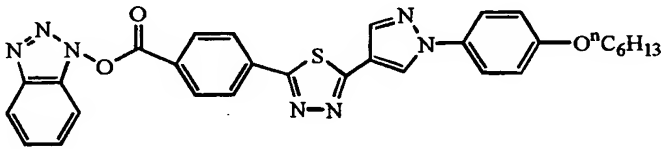
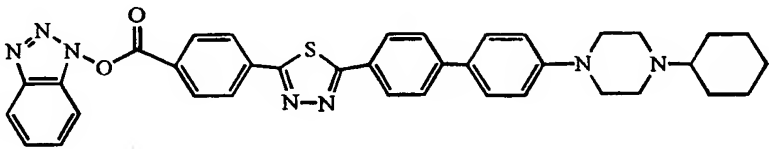
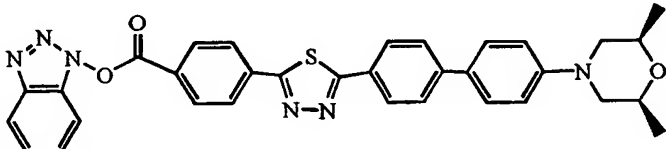
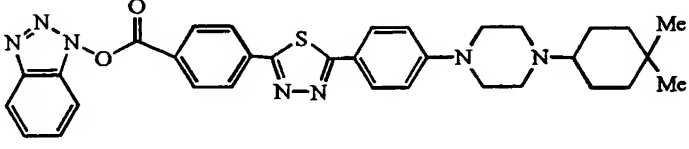
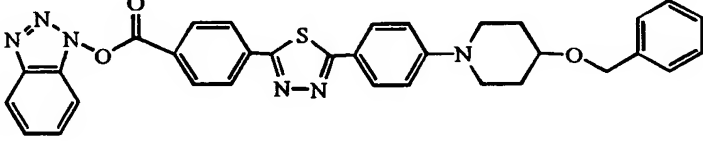
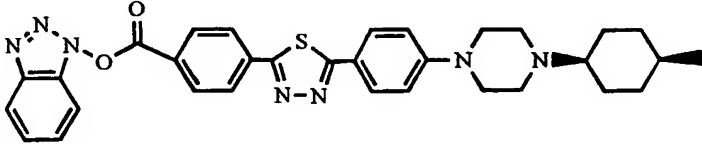
Preparation No.	Formula
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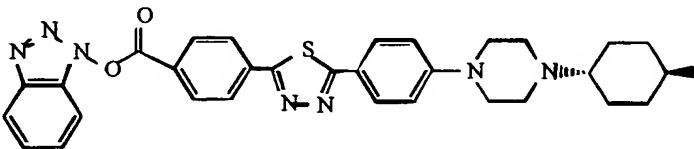
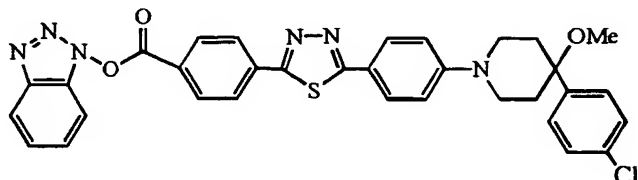
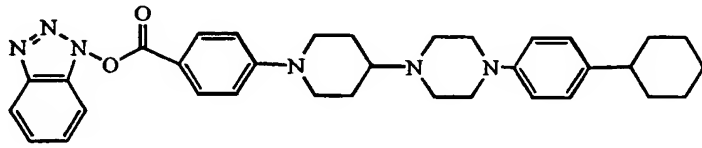
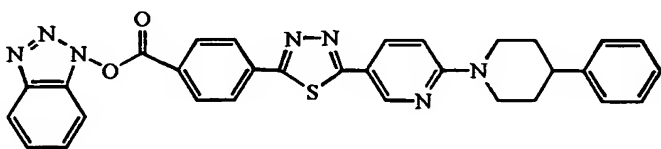
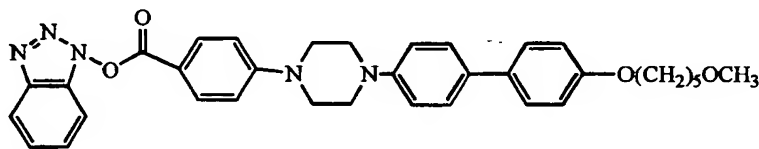
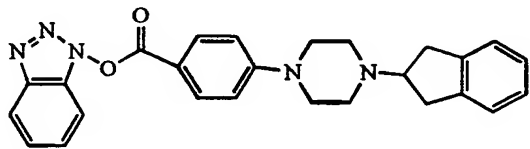
Preparation No.	Formula
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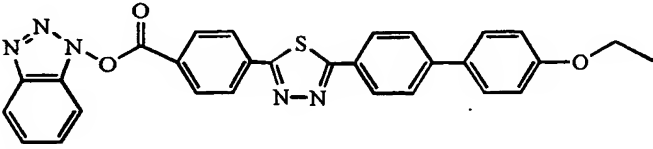
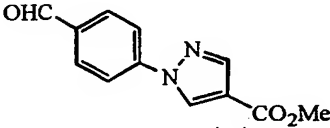
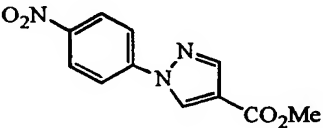
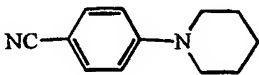
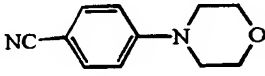
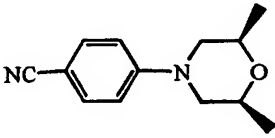
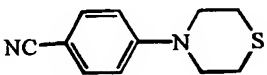
Preparation No.	Formula
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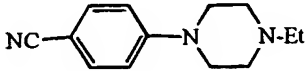
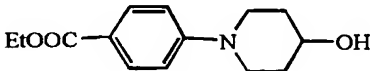
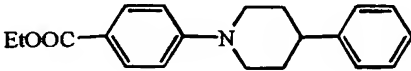
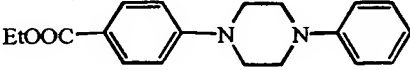
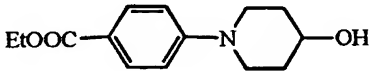
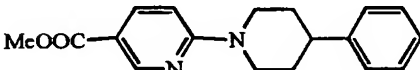
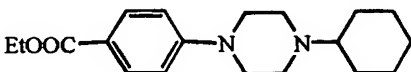
Preparation No.	Formula
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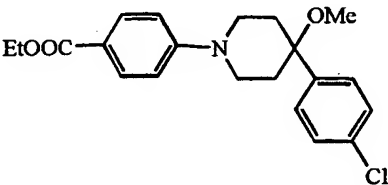
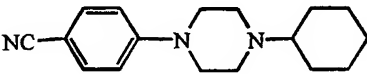
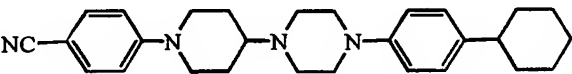
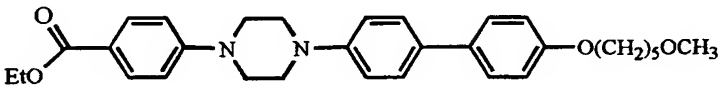
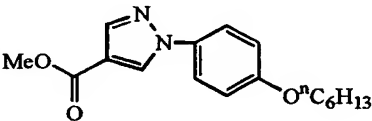
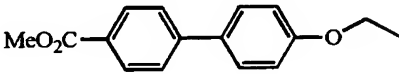



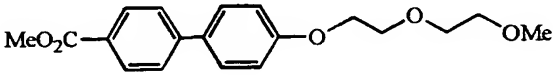
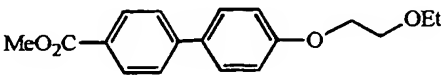
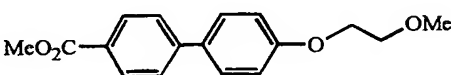
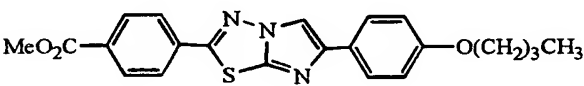
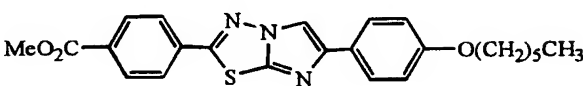
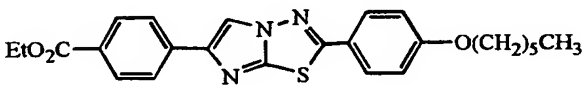
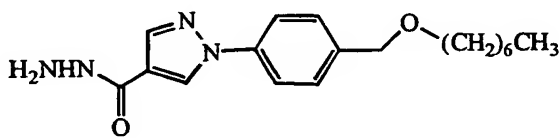
Preparation No.	Formula
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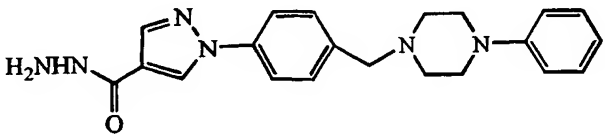
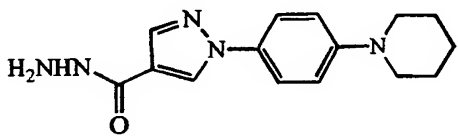
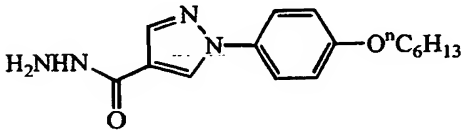
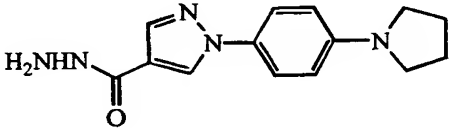
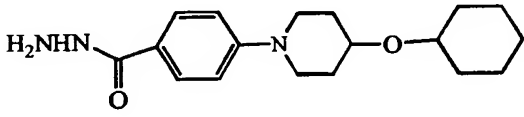
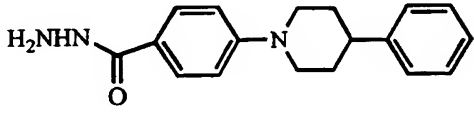
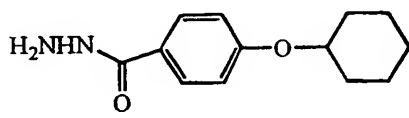
Preparation No.	Formula
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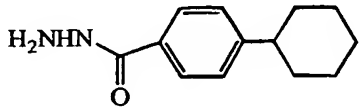
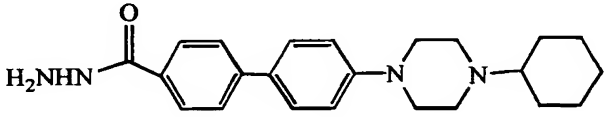
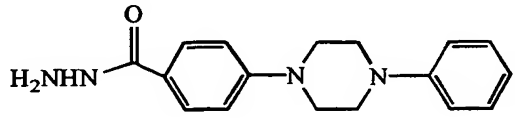
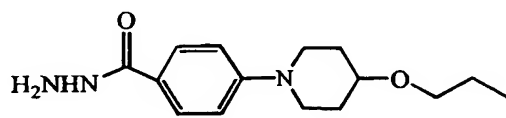
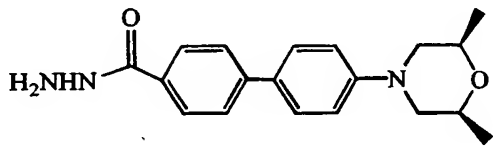
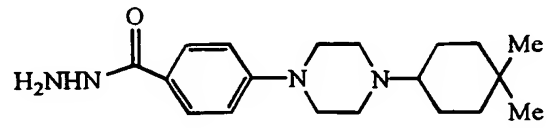
Preparation No.	Formula
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Preparation No.	Formula
260	 <chem>N#Cc1ccc(cc1)N2CCCC2</chem>
261	 <chem>CCOC(=O)c1ccc(cc1)N2CCCC2O</chem>
262	 <chem>CCOC(=O)c1ccc(cc1)N2CCCC2c3ccccc3</chem>
263	 <chem>CCOC(=O)c1ccc(cc1)N2CCCN(C2)c3ccccc3</chem>
264	 <chem>CCOC(=O)c1ccc(cc1)N2CCC(O)C2</chem>
265	 <chem>CCOC(=O)c1ccncc1N2CCCC2c3ccccc3</chem>
266	 <chem>CCOC(=O)c1ccc(cc1)N2CCCC2N3CCCCC3</chem>

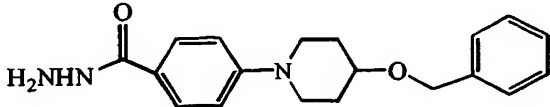
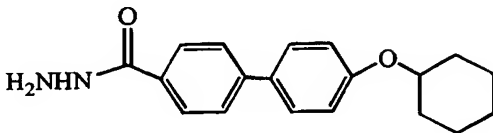
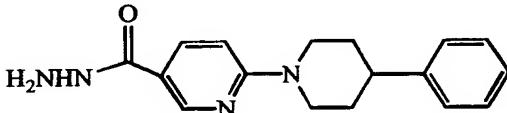
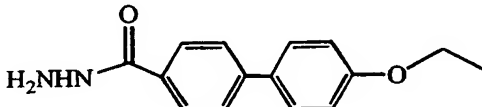
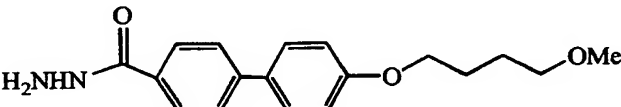
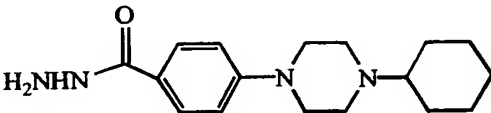
Preparation No.	Formula
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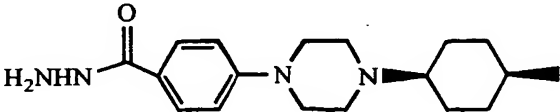
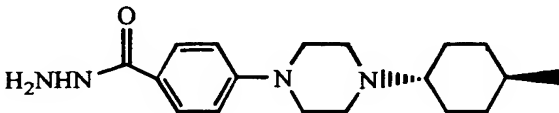
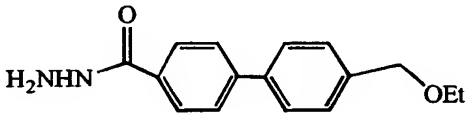
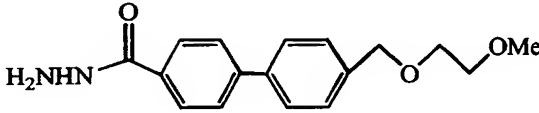
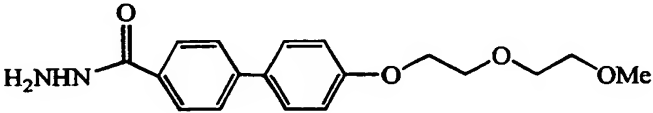
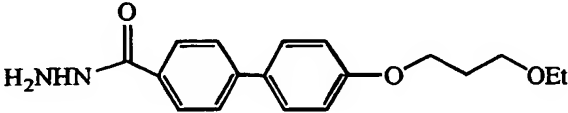
Preparation No.	Formula
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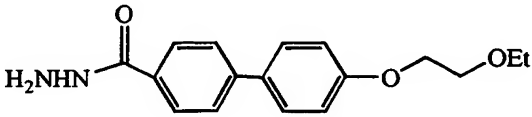
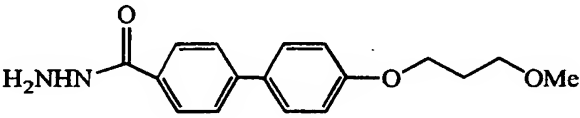
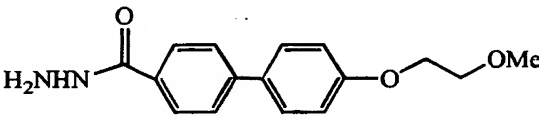
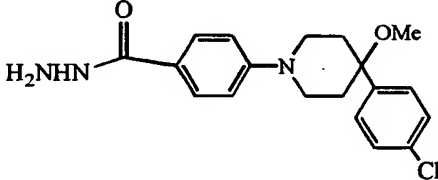
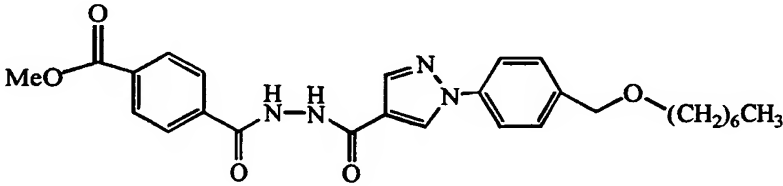
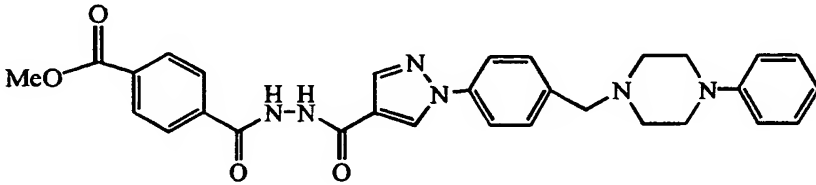
Preparation No.	Formula
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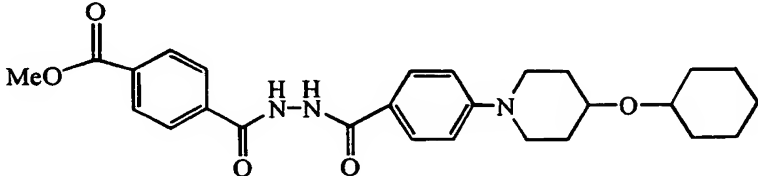
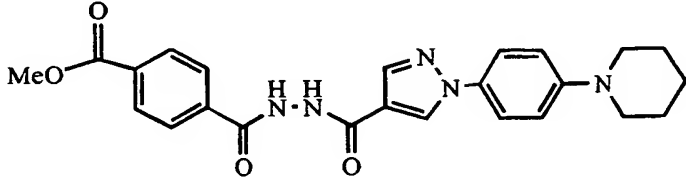
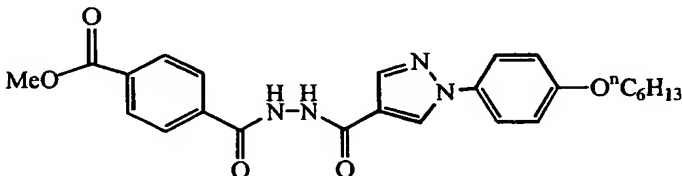
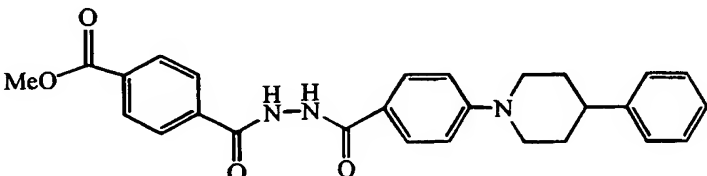
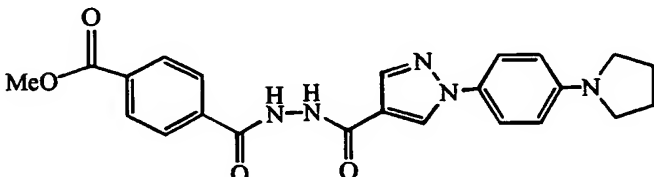
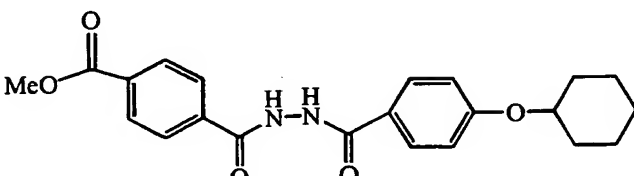
Preparation No.	Formula
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289	 <chem>NC(=O)c1ccc(cc1)-c2ccc(cc2)N3CCN(CC3)C4CCCCC4</chem>
290	 <chem>NC(=O)c1ccc(cc1)N2CCN(CC2)c3ccccc3</chem>
291	 <chem>NC(=O)c1ccc(cc1)N2CCN(CC2)OCC</chem>
292	 <chem>NC(=O)c1ccc(cc1)-c2ccc(cc2)N3CCOC(C)(C)C3</chem>
293	 <chem>NC(=O)c1ccc(cc1)N2CCN(CC2)C3CCCC(C)(C)C3</chem>

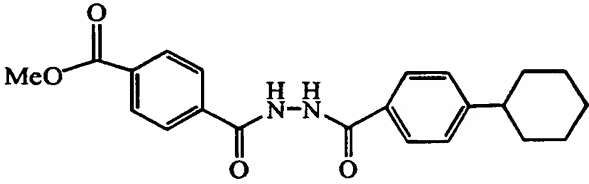
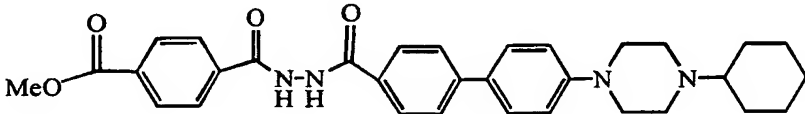
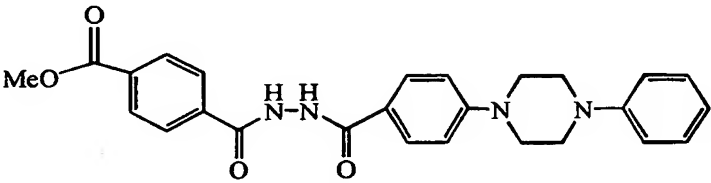
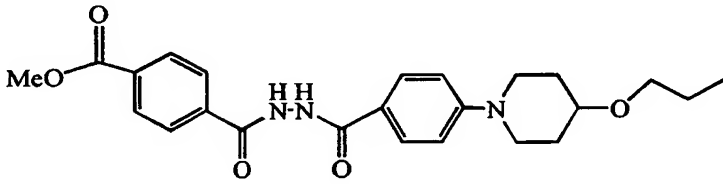
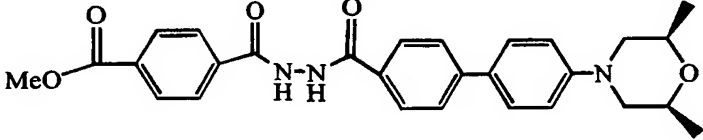
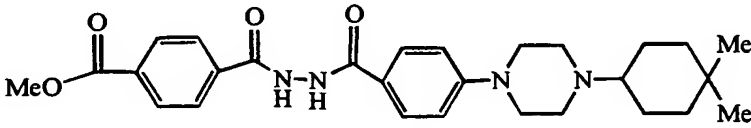


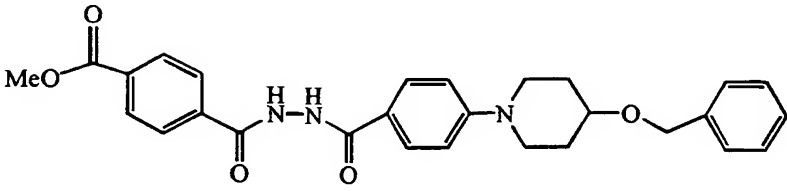
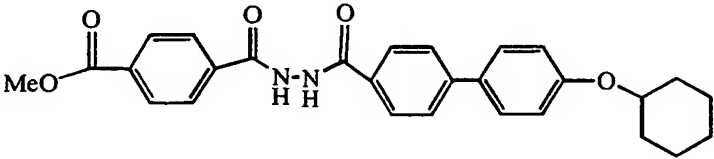
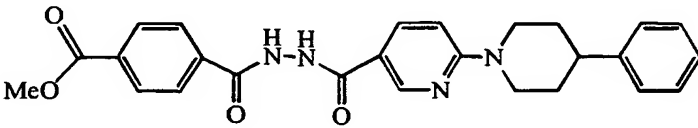
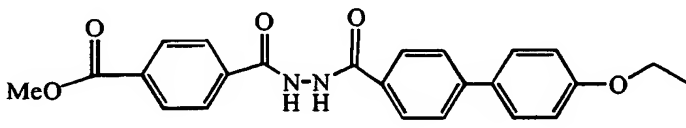
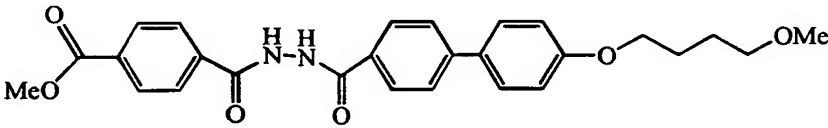
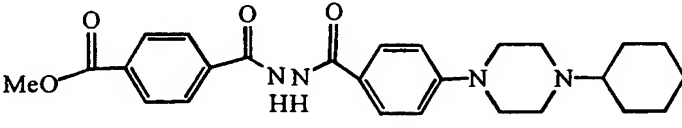
Preparation No.	Formula
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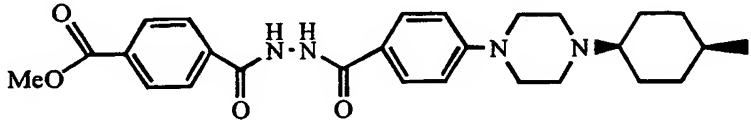
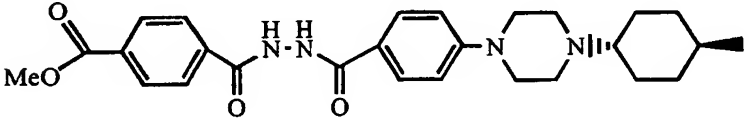
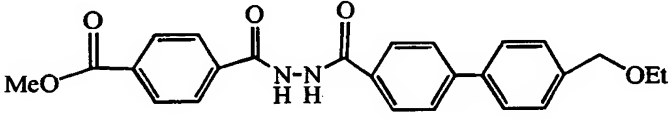
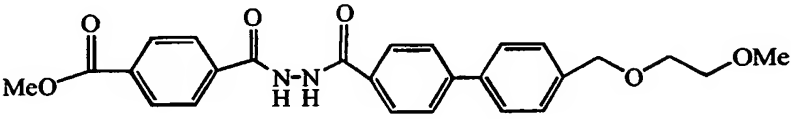
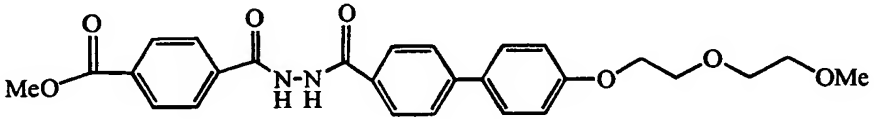
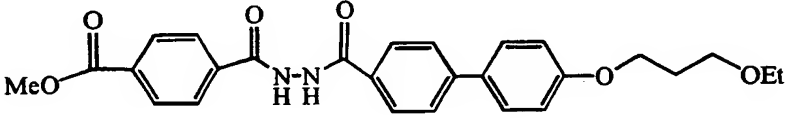
Preparation No.	Formula
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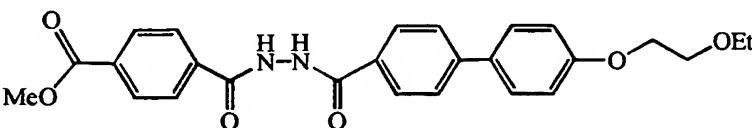
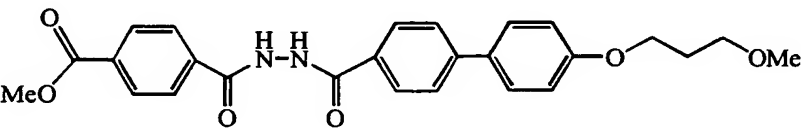
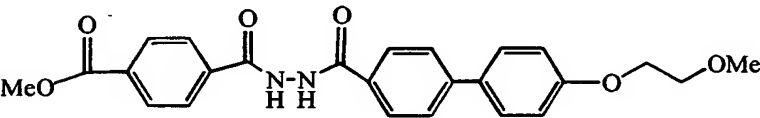
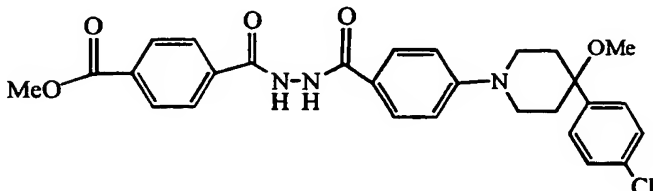
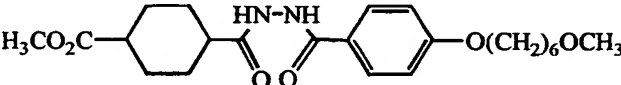
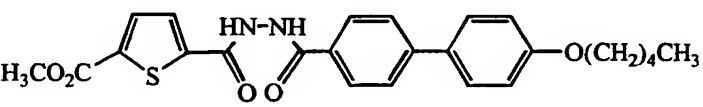
Preparation No.	Formula
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Preparation No.	Formula
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Preparation No.	Formula
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Preparation No.	Formula
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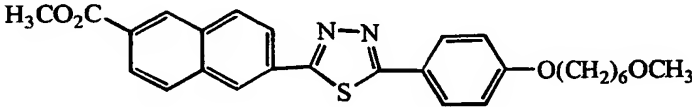
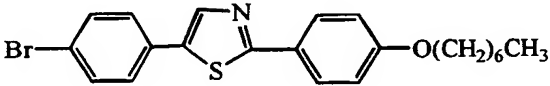
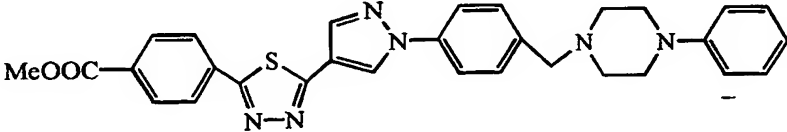
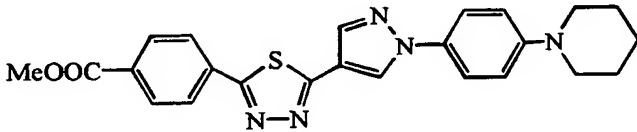
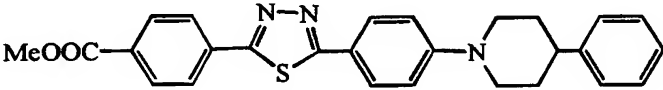
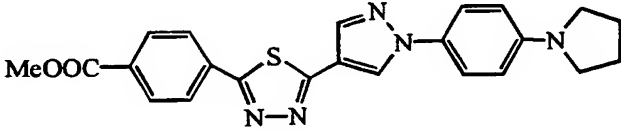
Preparation No.	Formula
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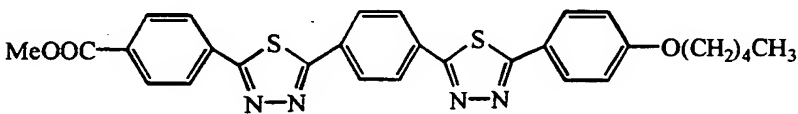
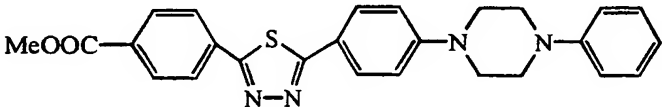
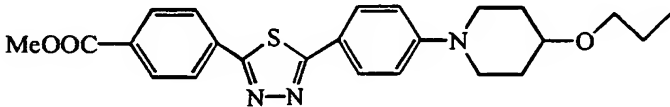
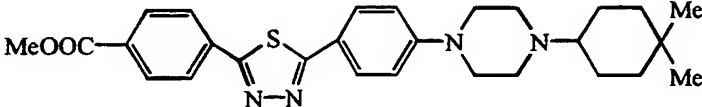
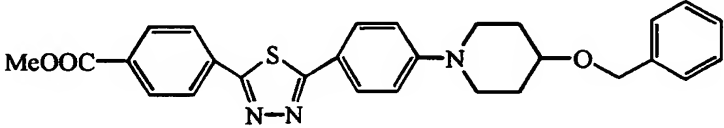
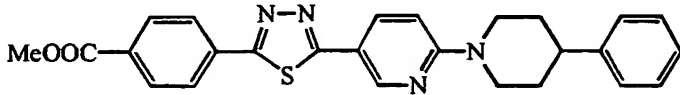
Preparation No.	Formula
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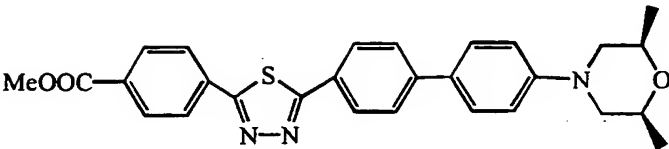
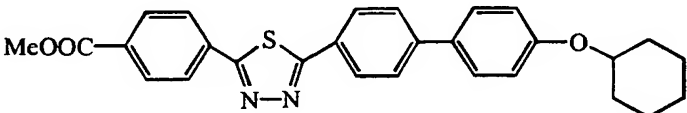
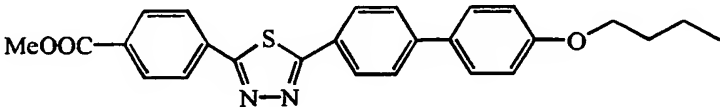
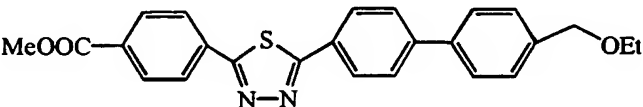
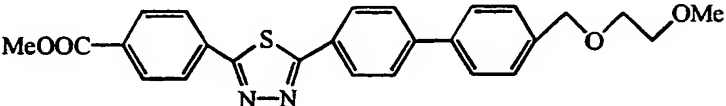
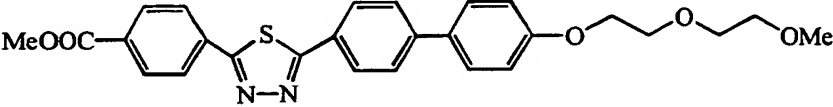
Preparation No.	Formula
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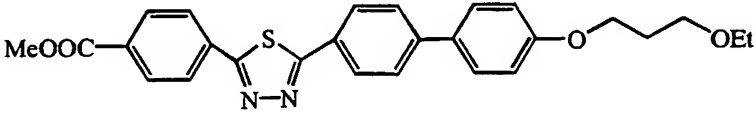
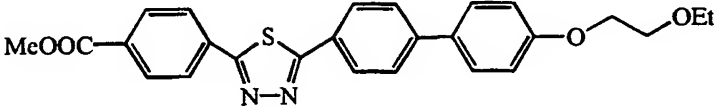
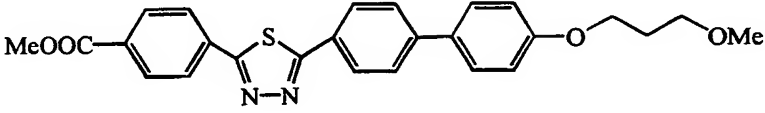
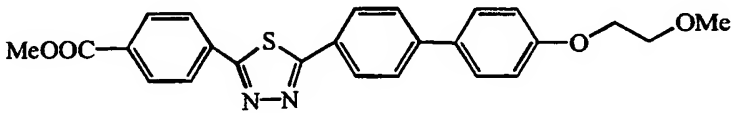
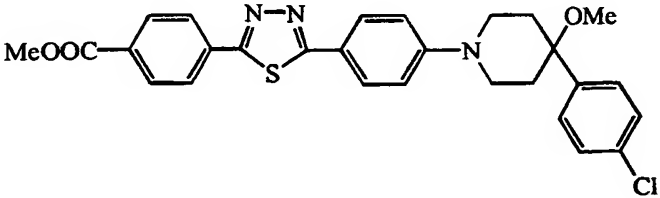
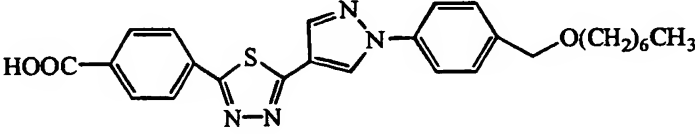
Preparation No.	Formula
348	<chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)C4CCCCC4</chem>
349	<chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)OC4CCCCC4</chem>
350	<chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccnn3-c4ccc(cc4)OC12CCCCCCCC12</chem>
351	<chem>COC(=O)C1CCCCC1-c2nn(s2)-c3ccc(cc3)OCCCCCOCC</chem>
352	<chem>COC(=O)c1cc(C)c(C)cc1-c2nn(s2)-c3ccc(cc3)OCCCCCOCC</chem>
353	<chem>COC(=O)/C=C/C=C/c1nn(s1)-c2ccc(cc2)OCCCCCOCC</chem>

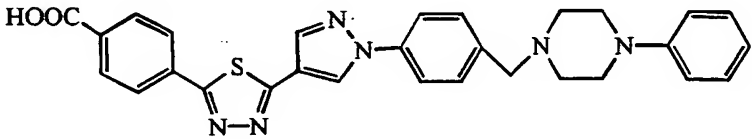
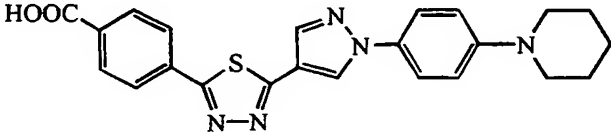
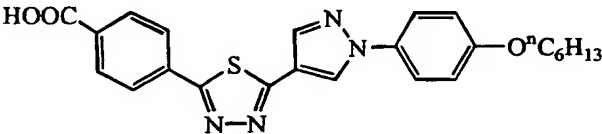
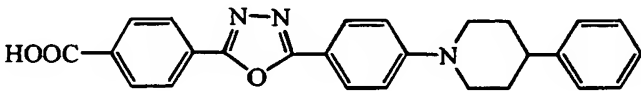
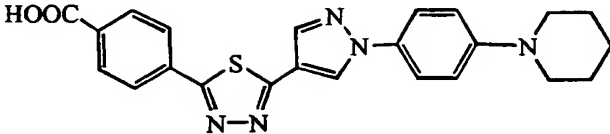
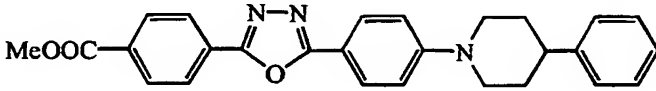
Preparation No.	Formula
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Preparation No.	Formula
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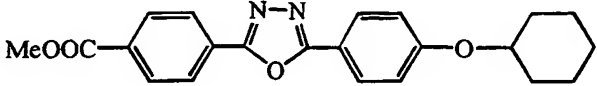
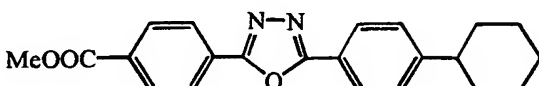
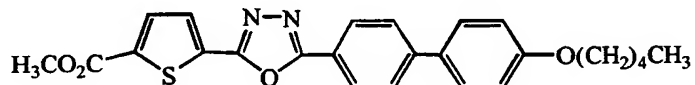
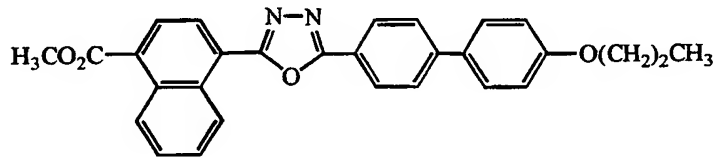
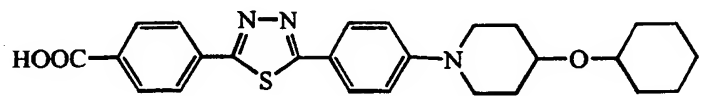
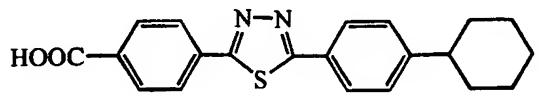
Preparation No.	Formula
366	 <chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)-c4ccc(OCCCCOC)cc4</chem>
367	 <chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)-N4CCN(CC4)C5CCCCC5</chem>
368	 <chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)-N4CCN(CC4)C5CCCC[C@H]5</chem>
369	 <chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)-N4CCN(CC4)C5CCCC[C@@H]5</chem>
370	 <chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)-c4ccc(OCC)cc4</chem>
371	 <chem>COC(=O)c1ccc(cc1)-c2nn(s2)-c3ccc(cc3)-c4ccc(cc4)-N5CCN(CC5)C6CCCCC6</chem>

Preparation No.	Formula
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Preparation No.	Formula
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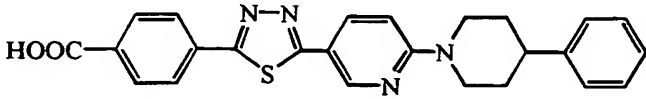
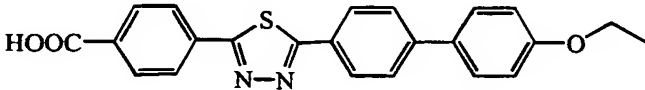
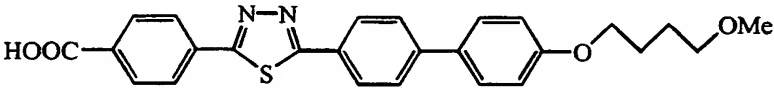
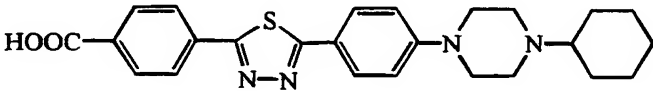
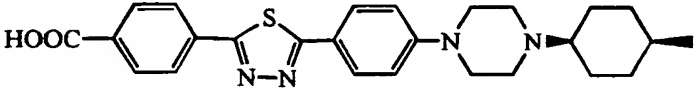
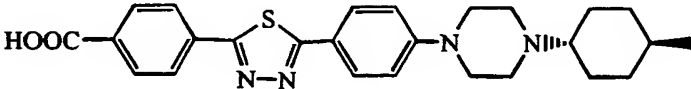
Preparation No.	Formula
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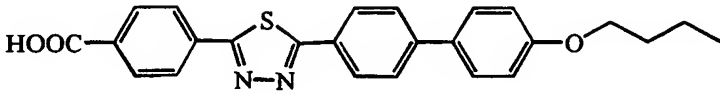
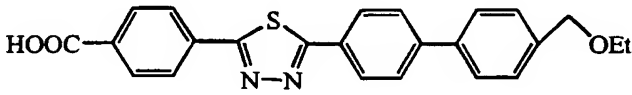
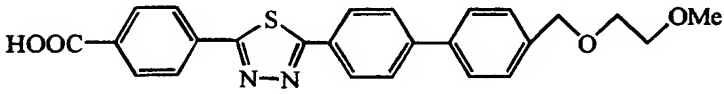
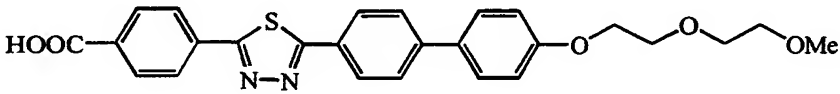
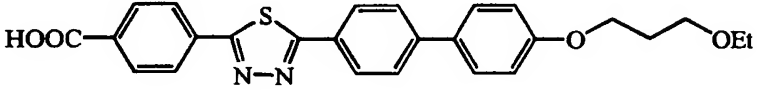
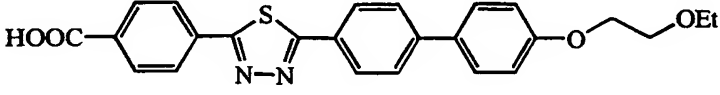


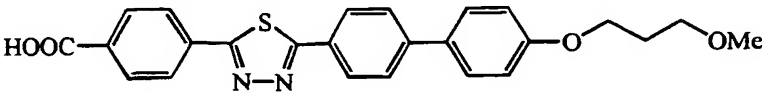
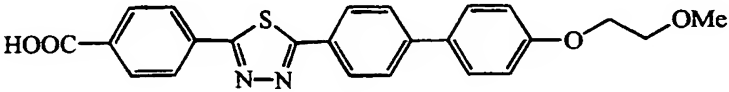
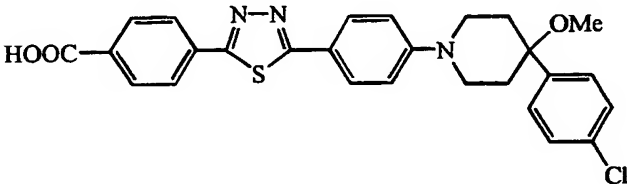
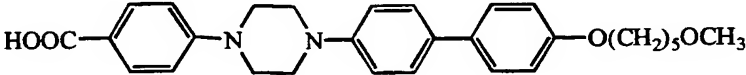
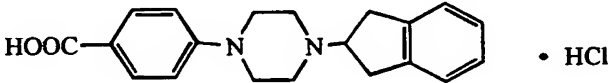
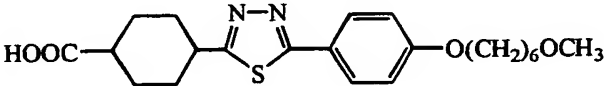
Preparation No.	Formula
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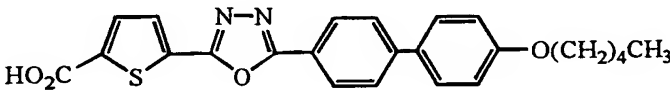
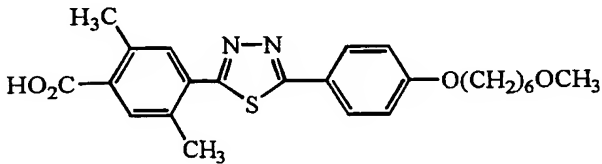
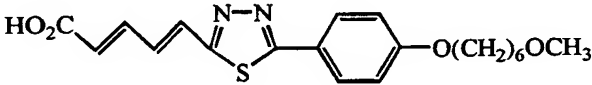
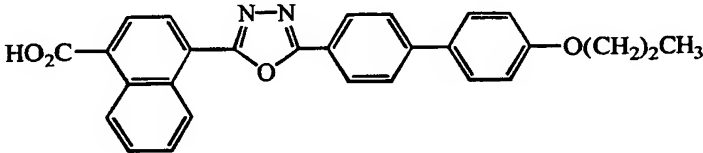
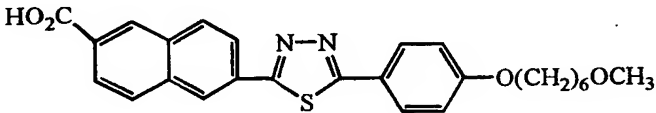
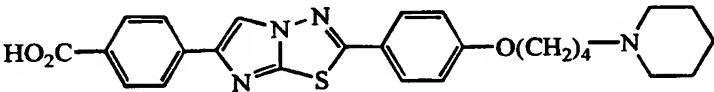
Preparation No.	Formula
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400	<p style="text-align: right;">• 2HCl</p>
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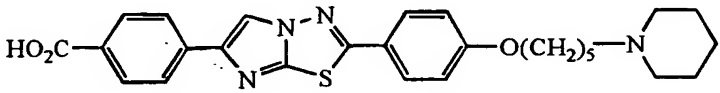
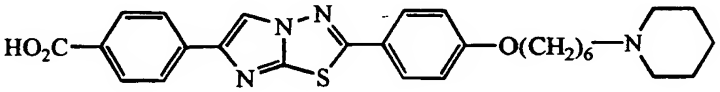
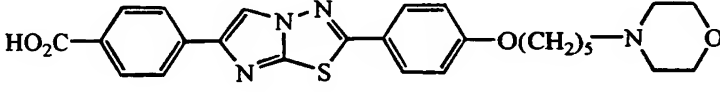
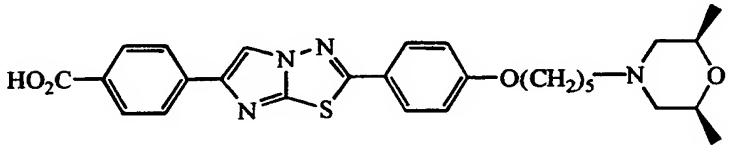
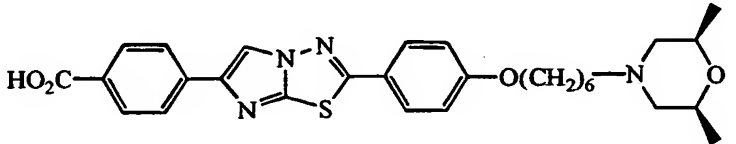
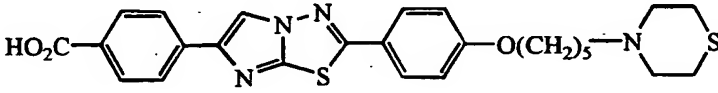
Preparation No.	Formula
402	<p>• 2HCl</p>
403	<p>• HCl</p>
404	<p>• HCl</p>
405	<p>• 2HCl</p>
406	<p>• HCl</p>
407	<p></p>

Preparation No.	Formula
408	 <p>• HCl</p>
409	
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411	 <p>• 2HCl</p>
412	 <p>• 2HCl</p>
413	 <p>• 2HCl</p>

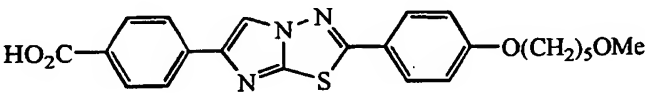
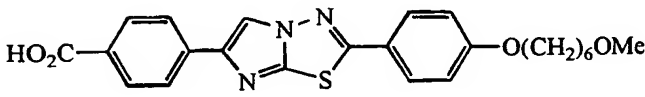
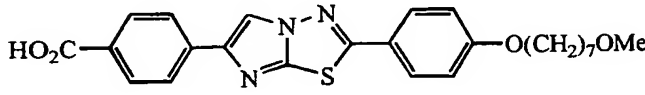
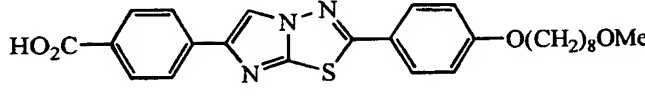
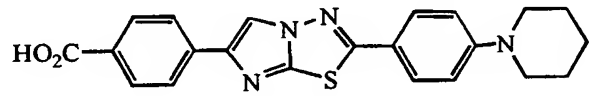
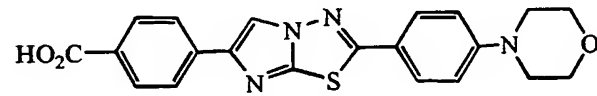
Preparation No.	Formula
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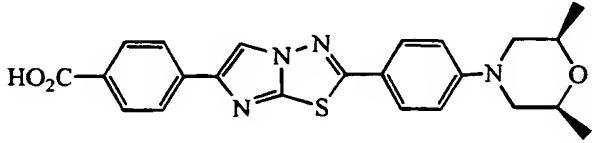
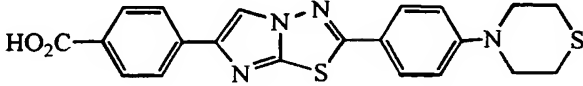
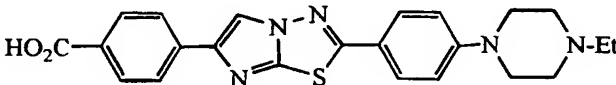
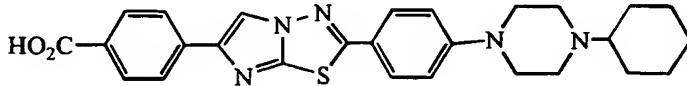
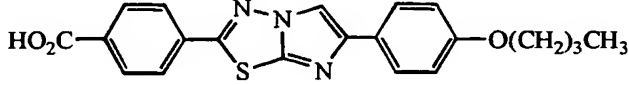
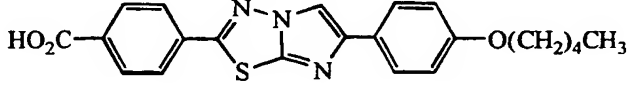
Preparation No.	Formula
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423	 • HCl
424	 • HCl
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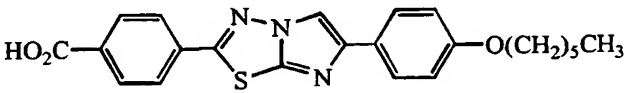
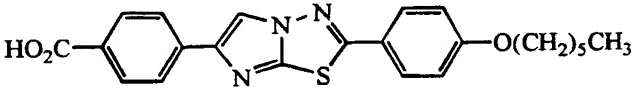
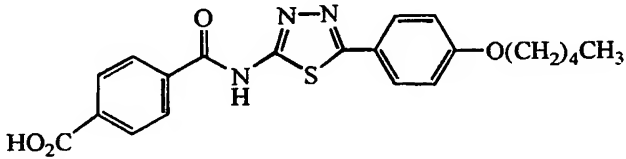
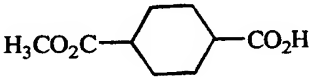
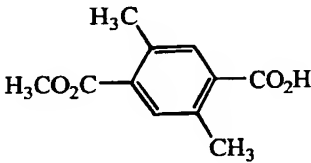
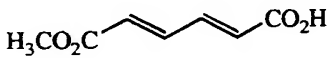
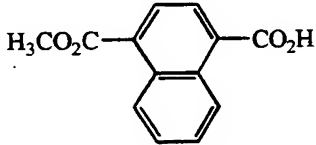
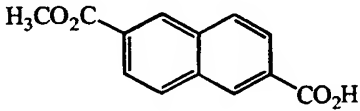
Preparation No.	Formula
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Preparation No.	Formula
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Preparation No.	Formula
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Preparation No.	Formula
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Preparation No.	Formula
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The following compounds [Preparations 211 to 253] were obtained in a manner similar to that of Preparation 18.

Preparation 211

5 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.10-1.45 (6H, m), 1.45-2.10 (8H, m),  
3.0-3.80 (6H, m), 6.97 (2H, d, J=9.0Hz), 7.40-7.65  
(3H, m), 7.90 (2H, d, J=8.9Hz), 8.13 (2H, d, J=8.2Hz),  
8.18 (2H, d, J=8.7Hz), 8.39 (2H, d, J=8.6Hz)

APCI MASS : 581 (M<sup>+</sup>)

Preparation 212

10 IR (KBr) : 3008, 2935, 1792, 1770, 1600 cm<sup>-1</sup>  
NMR (CDCl<sub>3</sub>,  $\delta$ ) : 3.97 (3H, s), 7.07 (2H, d, J=8.5Hz),  
7.43-7.56 (3H, m), 8.10 (1H, d, J=8.5Hz), 8.23 (2H,  
d, J=8.5Hz)

MASS (m/z) : 270 (M+H<sup>+</sup>)

15 Preparation 213

IR (KBr) : 1776, 1234, 1095 cm<sup>-1</sup>  
NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.89 (3H, m), 1.1-2.0 (10H, m),  
3.52 (2H, t, J=6.6Hz), 4.57 (2H, s), 7.4-7.6 (4H,  
m), 7.75 (2H, d, J=8.5Hz), 8.14 (2H, d, J=8.1Hz),  
20 8.22 (1H, s), 8.26 (2H, d, J=8.7Hz), 8.43 (2H, d,  
J=8.7Hz), 8.59 (1H, s)

MASS (m/z) : 594 (M<sup>+</sup>+1)

Preparation 214

25 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.20-1.60 (5H, m), 1.70-2.05 (5H, m),  
2.50-2.75 (1H, m), 7.25-8.50 (12H, m)

ESI MASS (positive) : 502.3 (M<sup>+</sup>+Na)

Preparation 215

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.10-2.20 (10H, m), 4.30-4.50 (1H, m),  
7.04 (2H, d, J=9.1Hz), 7.40-8.50 (10H, m)

30 APCI MASS (positive) : 518.3 (M<sup>+</sup>+Na)

Preparation 216

35 NMR (CDCl<sub>3</sub>+CD<sub>3</sub>OD,  $\delta$ ) : 1.70-2.15 (4H, m), 2.70-2.90  
(1H, m), 2.90-3.20 (2H, m), 4.00-4.15 (2H, m), 7.08  
(2H, d, J=9.1Hz), 7.10-7.40 (5H, m), 7.40-7.70 (3H,  
m), 7.90-8.55 (7H, m)

APCI MASS : 543 ( $M^+ + 1$ )

Preparation 217

NMR ( $CDCl_3 + CD_3OD$ ,  $\delta$ ) : 1.70-2.10 (4H, m), 2.60-3.15  
(3H, m), 3.90-4.15 (2H, m), 6.90-7.15 (2H, m),  
5 7.15-7.40 (6H, m), 7.40-8.45 (9H, m)

Preparation 218

NMR ( $CDCl_3$ ,  $\delta$ ) : 1.20-2.15 (10H, m), 4.25-4.50 (1H, m),  
7.05 (2H, d,  $J=6.9Hz$ ), 7.35-7.65 (3H, m), 8.00-8.50  
(7H, m)

10 APCI MASS (positive) : 502.2 ( $M^+ + Na$ )

Preparation 219

NMR ( $CDCl_3$ ,  $\delta$ ) : 1.15-2.00 (10H, m), 2.45-2.75 (1H, m),  
7.30-8.50 (12H, m)

APCI MASS (positive) : 466.2 ( $M^+ + 1$ )

15 Preparation 220

IR (KBr) : 2978, 2937, 2873, 1772, 1599, 1498,  
1439  $cm^{-1}$

NMR ( $CDCl_3$ ,  $\delta$ ) : 1.27 (3H, t,  $J=7.0Hz$ ), 3.65 (2H, q,  
 $J=7.0Hz$ ), 3.84 (2H, t,  $J=4.8Hz$ ), 4.20 (2H, t,  
20  $J=4.8Hz$ ), 7.05 (2H, d,  $J=8.8Hz$ ), 7.40-7.66 (5H, m),  
7.60 (2H, d,  $J=8.8Hz$ ), 7.72 (2H, d,  $J=8.4Hz$ ),  
8.07-8.17 (1H, m), 8.28 (2H, d,  $J=8.6Hz$ ), 8.43 (2H,  
d,  $J=8.7Hz$ )

MASS (m/z) : 564 ( $M^+ + 1$ )

25 Preparation 221

IR (KBr) : 1778.0, 1600.6, 1230.4, 1182.2  $cm^{-1}$   
NMR ( $CDCl_3$ ,  $\delta$ ) : 1.10-1.74 (10H, m), 2.82 (2H, t,  $J=7.2Hz$ ),  
3.33 (3H, s), 3.33-3.65 (10H, m), 6.88-7.02 (4H, m),  
7.32-7.58 (5H, m), 8.07-8.18 (3H, m)

30 Preparation 222

IR (KBr) : 1810.8, 1600.6, 1257.4, 1178.3  $cm^{-1}$   
NMR ( $DMSO-d_6$ ,  $\delta$ ) : 1.30-2.40 (18H, m), 3.21 (3H, s),  
3.28-3.35 (2H, m), 4.05 (2H, t,  $J=6.6Hz$ ), 7.05-7.10  
(2H, m), 7.40-8.18 (6H, m)

35 MASS (m/z) : 536 ( $M + 1$ )

Preparation 223IR (KBr) : 1776.1, 1677.8, 1251.6, 1197.6  $\text{cm}^{-1}$ NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=6.9\text{Hz}$ ), 1.23-1.55

(4H, m), 1.60-1.90 (2H, m), 4.00-4.10 (2H, m),

5 7.03-7.09 (2H, m), 7.39-8.17 (12H, m)

MASS ( $m/z$ ) : 552Preparation 224

IR (KBr) : 1795.4, 1606.4, 1442.5, 1259.3,

1220.7  $\text{cm}^{-1}$ 10 NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 1.44-1.95 (8H, m), 2.71 (3H, s),2.75 (3H, s), 3.35 (3H, s), 3.40 (2H, t,  $J=6.4\text{Hz}$ ),4.05 (2H, t,  $J=6.4\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ),

7.43-7.64 (3H, m), 7.84 (1H, s), 7.96-8.15 (3H, m),

8.34 (1H, s)

15 MASS ( $m/z$ ) : 558 ( $M+1$ )Preparation 225IR (KBr) : 1697.1, 1604.5, 1251.6  $\text{cm}^{-1}$ NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.40-2.00 (8H, m), 3.35 (3H, s),3.40 (2H, t,  $J=6.4\text{Hz}$ ), 4.04 (2H, t,  $J=6.4\text{Hz}$ ),

20 6.97-7.02 (2H, m), 7.20-8.07 (9H, m), 8.50-8.54 (1H, m)

MASS ( $m/z$ ) : 506 ( $M+1$ )Preparation 226IR (KBr) : 1778.0, 1602.6, 1238.1  $\text{cm}^{-1}$ 25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.07 (3H, t,  $J=7.4\text{Hz}$ ), 1.77-1.94 (2H,m), 4.00 (2H, t,  $J=6.6\text{Hz}$ ), 7.00-7.05 (2H, m),

7.46-9.56 (16H, m)

MASS ( $m/z$ ) : 568 ( $M+1$ )Preparation 22730 IR (KBr) : 1778.0, 1604.5, 1257.4, 1172.5  $\text{cm}^{-1}$ NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.40-1.90 (8H, m), 3.35 (3H, s), 3.41(2H, t,  $J=6.3\text{Hz}$ ), 4.05 (2H, t,  $J=6.3\text{Hz}$ ), 7.00-7.04

(2H, m), 7.44-9.04 (12H, m)

MASS ( $m/z$ ) : 580 ( $M+1$ )

Preparation 228

IR (KBr) : 2956, 2933, 2872, 1776, 1601, 1500,  
1438  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00 (3H, t,  $J=7.3\text{Hz}$ ), 1.40-1.96  
(4H, m), 4.04 (2H, t,  $J=6.5\text{Hz}$ ), 7.02 (2H, d,  $J=8.7\text{Hz}$ ),  
7.36-7.66 (5H, m), 7.73 (2H, d,  $J=8.4\text{Hz}$ ), 8.00-8.21  
(3H, m), 8.28 (2H, d,  $J=8.6\text{Hz}$ ), 8.44 (2H, d,  $J=8.7\text{Hz}$ )  
MASS (m/z) : 548 ( $M^+ + 1$ )

Preparation 229

10 IR (KBr) : 2870, 1778, 1649, 1601, 1529, 1500, 1471,  
1439  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.70-2.00 (4H, m), 3.37 (3H, s),  
3.47 (2H, t,  $J=6.1\text{Hz}$ ), 4.06 (2H, t,  $J=6.1\text{Hz}$ ), 7.01  
(2H, d,  $J=8.7\text{Hz}$ ), 7.42-7.68 (3H, m), 7.60 (2H, d,  
15  $J=8.8\text{Hz}$ ), 7.72 (2H, d,  $J=8.5\text{Hz}$ ), 8.06-8.20 (1H, m),  
8.28 (2H, d,  $J=8.7\text{Hz}$ ), 8.43 (2H, d,  $J=8.6\text{Hz}$ )  
MASS (m/z) : 578 ( $M^+ + 1$ )

Preparation 230

20 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.29 (3H, t,  $J=7.0\text{ Hz}$ ), 3.60 (2H, q,  
 $J=7.0\text{Hz}$ ), 4.58 (2H, s), 7.40-7.64 (5H, m), 7.65  
(2H, d,  $J=8.2\text{Hz}$ ), 7.76 (2H, d,  $J=8.4\text{Hz}$ ), 8.09-8.20  
(3H, m), 8.29 (2H, d,  $J=8.7\text{Hz}$ ), 8.44 (2H, d,  $J=8.7\text{Hz}$ )  
MASS (m/z) : 534 ( $M^+ + 1$ )

Preparation 231

25 IR (KBr) : 2978, 2937, 2873, 1772, 1599, 1498,  
1439  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.42 (3H, m), 3.55-3.74 (4H, m), 4.65  
(2H, s), 7.43-7.63 (5H, m), 7.65 (2H, d,  $J=8.2\text{Hz}$ ),  
7.76 (2H, d,  $J=8.5\text{Hz}$ ), 8.08-8.17 (3H, m), 8.28 (2H,  
30 d,  $J=8.7\text{Hz}$ ), 8.43 (2H, d,  $J=8.6\text{Hz}$ )  
MASS (m/z) : 564 ( $M^+ + 1$ )

Preparation 232

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.41 (3H, s), 3.54-3.68 (2H, m), 3.68-3.80  
(2H, m), 3.90 (2H, t,  $J=4.9\text{Hz}$ ), 4.22 (2H, t,  $J=4.9\text{Hz}$ ),  
7.04 (2H, d,  $J=8.8\text{Hz}$ ), 7.44-7.68 (3H, m), 7.55 (2H,

d,  $J=9.1\text{Hz}$ ), 7.72 (2H, d,  $J=8.5\text{Hz}$ ), 8.05-8.20 (3H, m), 8.27 (2H, d,  $J=8.6\text{Hz}$ ), 8.43 (2H, d,  $J=8.7\text{Hz}$ )

MASS ( $m/z$ ) : 594 ( $M^+ + 1$ )

Preparation 233

5 IR (KBr) : 2976, 2868, 1778, 1601, 1527, 1500, 1471, 1439  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.22 (3H, t,  $J=7.0\text{Hz}$ ), 2.10 (2H, m), 3.52 (2H, q,  $J=7.0\text{Hz}$ ), 3.63 (2H, t,  $J=6.2\text{Hz}$ ), 4.14 (2H, t,  $J=6.5\text{Hz}$ ), 7.03 (2H, d,  $J=8.8\text{Hz}$ ), 7.42-7.66 (5H, m), 7.72 (2H, d,  $J=8.5\text{Hz}$ ), 8.04-8.20 (1H, m), 8.10 (2H, d,  $J=8.4\text{Hz}$ ), 8.28 (2H, d,  $J=8.6\text{Hz}$ ), 8.43 (2H, d,  $J=8.6\text{Hz}$ )

Preparation 234

15 IR (KBr) : 2926, 2877, 1768, 1601, 1527, 1500, 1439, 1417  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.09 (2H, m), 3.38 (3H, s), 3.59 (2H, t,  $J=6.1\text{Hz}$ ), 4.13 (2H, t,  $J=6.3\text{Hz}$ ), 7.03 (2H, d,  $J=8.8\text{Hz}$ ), 7.44-7.66 (5H, m), 7.72 (2H, d,  $J=8.5\text{Hz}$ ), 8.08-8.18 (3H, m), 8.28 (2H, d,  $J=8.7\text{Hz}$ ), 8.44 (2H, d,  $J=8.7\text{Hz}$ )

20 MASS ( $m/z$ ) : 564 ( $M^+ + 1$ )

Preparation 235

IR (KBr) : 1776, 1655, 1601, 1529, 1498, 1439  $\text{cm}^{-1}$

25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.49 (3H, s), 3.80 (2H, m), 4.20 (2H, m), 7.05 (2H, d,  $J=8.8\text{Hz}$ ), 7.40-7.64 (4H, m), 7.72 (2H, d,  $J=8.4\text{Hz}$ ), 7.98-8.18 (4H, m), 8.28 (2H, d,  $J=8.6\text{Hz}$ ), 8.44 (2H, d,  $J=8.7\text{Hz}$ )

MASS ( $m/z$ ) : 550 ( $M^+ + 1$ )

Preparation 236

30 IR (KBr) : 1776, 1603, 1527, 1497, 1439  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.19-2.14 (10H, m), 4.23-4.40 (1H, m), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.41-7.67 (5H, m), 7.72 (2H, d,  $J=8.5\text{Hz}$ ), 8.02-8.21 (3H, m), 8.28 (2H, d,  $J=8.7\text{Hz}$ ), 8.43 (2H, d,  $J=8.7\text{Hz}$ )

35 MASS ( $m/z$ ) : 574 ( $M^+ + 1$ )



Preparation 237

IR (KBr) : 2929.3, 2856.1, 1774.2, 1602.6,  
1253.5  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.80-1.10 (3H, m), 1.10-1.60 (8H, m),  
1.60-2.00 (2H, m), 4.03 (2H, t,  $J=6.5\text{Hz}$ ), 6.98 (2H,  
d,  $J=8.8\text{Hz}$ ), 7.40-7.70 (3H, m), 7.81 (2H, d,  
 $J=8.5\text{Hz}$ ), 7.93 (2H, d,  $J=8.8\text{Hz}$ ), 8.12 (2H, d,  
 $J=8.1\text{Hz}$ ), 8.17 (1H, s), 8.31 (2H, d,  $J=8.5\text{Hz}$ )

APCI MASS ( $m/z$ ) : 513

10 Preparation 238

IR (KBr) : 1776, 1603, 1524, 1441, 1414  $\text{cm}^{-1}$

15 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.03-1.43 (5H, m), 1.54-2.14 (5H, m),  
2.24-2.50 (1H, m), 2.65-2.86 (4H, m), 3.23-3.47 (4H,  
m), 6.98 (2H, d,  $J=8.7\text{Hz}$ ), 7.41-7.68 (3H, m), 7.92  
(2H, d,  $J=8.5\text{Hz}$ ), 8.13 (1H, d,  $J=8.2\text{Hz}$ ), 8.24 (2H,  
d,  $J=8.2\text{Hz}$ ), 8.40 (2H, d,  $J=8.2\text{Hz}$ )

MASS ( $m/z$ ) : 566 ( $M^+ + 1$ )

Preparation 239

IR (KBr) : 1772, 1574, 1234  $\text{cm}^{-1}$

20 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.6-2.75 (4H, m), 3.2-3.3 (4H, m),  
3.65 (2H, s), 6.8-7.0 (3H, m), 7.1-7.3 (2H, m),  
7.4-7.6 (4H, m), 7.74 (2H, d,  $J=8.5\text{Hz}$ ), 8.14 (2H,  
d,  $J=8.1\text{Hz}$ ), 8.21 (1H, s), 8.26 (2H, d,  $J=8.6\text{Hz}$ ),  
8.43 (2H, d,  $J=8.6\text{Hz}$ ), 8.59 (1H, s)

25 MASS ( $m/z$ ) : 640 ( $M^+ + 1$ )

Preparation 240

IR (KBr) : 1780, 1520, 1236, 982  $\text{cm}^{-1}$

30 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.5-1.8 (6H, m), 3.42 (4H, t,  $J=5.6\text{Hz}$ ),  
7.02 (2H, d,  $J=9.1\text{Hz}$ ), 7.4-7.7 (5H, m), 8.14 (2H,  
d,  $J=10.5\text{Hz}$ ), 8.25 (2H, d,  $J=8.6\text{Hz}$ ), 8.42 (2H, d,  
 $J=8.6\text{Hz}$ ), 8.47 (1H, s)

MASS ( $m/z$ ) : 549 ( $M^+ + 1$ )

Preparation 241

IR (KBr) : 1776, 1571, 1252  $\text{cm}^{-1}$

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.8-1.0 (3H, m), 1.2-1.8 (8H, m),

4.02 (2H, t, J=6.5Hz), 7.01 (2H, d, J=9.0Hz),  
7.4-7.7 (5H, m), 8.1-8.3 (4H, m), 8.43 (2H, d,  
J=8.6Hz), 8.51 (1H, s)

Preparation 242

5 IR (KBr) : 2927, 2854, 1599, 1531, 1498, 1444  $\text{cm}^{-1}$   
MASS (m/z) : 642 ( $\text{M}^+ + 1$ )

Preparation 243

IR (KBr) : 1782, 1597, 1533, 1502, 1444, 1421  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.30 (6H, d, J=6.3Hz), 2.40-2.58  
10 (2H, m), 3.49-3.63 (2H, m), 3.72-3.94 (2H, m), 7.01  
(2H, d, J=8.8Hz), 7.42-7.65 (5H, m), 7.73 (2H, d,  
J=8.5Hz), 8.09 (2H, d, J=8.6Hz), 8.14 (1H, d,  
J=8.4Hz), 8.28 (2H, d, J=8.6Hz), 8.44 (2H, d,  
J=8.6Hz)  
15 MASS (m/z) : 589 ( $\text{M}^+ + 1$ )

Preparation 244

IR (KBr) : 1778, 1603, 1441, 1414  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.92 (6H, s), 1.10-1.84 (8H, m),  
2.16-2.35 (1H, m), 2.68-2.87 (4H, m), 3.30-3.46 (4H,  
20 m), 6.98 (2H, d, J=9.0Hz), 7.40-7.65 (3H, m), 7.93  
(2H, d, J=8.8Hz), 8.13 (1H, d, J=8.1Hz), 8.25 (2H,  
d, J=8.7Hz), 8.40 (2H, d, J=8.6Hz)  
MASS (m/z) : 594 ( $\text{M}^+ + 1$ )

Preparation 245

25 IR (KBr) : 1784, 1603, 1520, 1441, 1414  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.66-2.14 (4H, m), 3.07-3.28 (2H, m),  
3.56-3.84 (3H, m), 4.60 (2H, s), 6.98 (2H, d,  
J=9.0Hz), 7.23-7.67 (8H, m), 7.91 (2H, d, J=8.9Hz),  
8.13 (1H, d, J=8.2Hz), 8.23 (2H, d, J=8.6Hz), 8.40  
30 (2H, d, J=8.6Hz)  
MASS (m/z) : 589 ( $\text{M}^+ + 1$ )

Preparation 246

IR (KBr) : 1780, 1603, 1522, 1441, 1414  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, d, J=6.9Hz),  
35 1.37-2.15 (9H, m), 2.25-2.44 (1H, m), 2.68-2.92

(4H, m), 3.27-3.50 (4H, m), 6.98 (2H, d, J=9.0Hz),  
7.37-7.67 (3H, m), 7.93 (2H, d, J=8.9Hz), 8.08-8.18  
(1H, m), 8.24 (2H, d, J=8.6Hz), 8.40 (2H, d, J=8.6Hz)

Preparation 247

5 IR (KBr) : 1778, 1603, 1524, 1441, 1414  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.90 (3H, d, J=6.4Hz), 0.90-1.13 (2H,  
m), 1.13-2.05 (7H, m), 2.20-2.48 (1H, m), 2.62-2.90  
(4H, m), 3.23-3.53 (4H, m), 6.97 (2H, d, J=9.0Hz),  
7.38-7.66 (3H, m), 7.92 (2H, d, J=8.8Hz), 8.06-8.17  
10 (1H, m), 8.24 (2H, d, J=8.6Hz), 8.40 (2H, d, J=8.7Hz)

Preparation 248

IR (Nujol) : 1782, 1603  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.9-2.3 (4H, m), 3.03 (3H, s), 3.2-3.5  
(2H, m), 3.6-3.9 (2H, m), 7.03 (2H, d, J=8.9Hz), 7.36  
15 (4H, s), 7.4-7.7 (3H, m), 7.93 (2H, d, J=8.9Hz), 8.13  
(1H, d, J=8.2Hz)  
(+)APCI MASS : 623 ( $\text{M}+\text{H}$ )<sup>+</sup>

Preparation 249

IR (KBr) : 2923, 2848, 2823, 1766, 1602, 1515, 1450,  
20 1378, 1259, 1222, 1186, 1153, 1089, 1014,  
971  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.2-1.5 (5H, m), 1.6-1.9 (7H, m),  
2.07 (2H, m), 2.43 (1H, m), 2.6-2.9 (5H, m), 3.02  
(2H, t, J=8.5Hz), 3.26 (4H, m), 4.07 (2H, d, J=13Hz),  
25 6.8-7.1 (4H, m), 7.12 (2H, d, J=8.6Hz), 7.3-7.6 (3H,  
m), 8.0-8.2 (3H, m)  
MASS ( $m/z$ ) : 462 ( $\text{M}+\text{H}$ )<sup>+</sup>

Preparation 250

IR (KBr) : 1780, 1682, 1655, 1601, 1549, 1498, 1429  $\text{cm}^{-1}$   
30 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.62-1.95 (2H, m), 2.01 (2H, m),  
2.70-3.18 (3H, m), 4.64 (2H, m), 6.80 (1H, d,  
J=9.1Hz), 7.18-7.40 (5H, m), 7.40-7.65 (3H, m),  
8.00-8.25 (2H, m), 8.25 (2H, d, J=8.6Hz), 8.41 (2H,  
d, J=8.6Hz), 8.76 (1H, d, J=2.3Hz)  
35 MASS ( $m/z$ ) : 560 ( $\text{M}^++1$ )

Preparation 251IR (KBr) : 1781.9, 1602.6, 1228.4  $\text{cm}^{-1}$ NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.54-1.87 (6H, m), 3.35 (3H, s),3.38-3.68 (10H, m), 4.00 (2H, t,  $J=6.4\text{Hz}$ ), 6.93-7.05

5 (6H, m), 7.39-7.53 (7H, m), 8.08-8.18 (3H, m)

Preparation 252IR (KBr) : 1776.1, 1600.6, 1232.3  $\text{cm}^{-1}$ NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.73-2.78 (4H, m), 2.93-3.73 (9H, m),

6.94-6.98 (2H, m), 7.14-7.58 (7H, m), 8.07-8.15 (3H,

10 m)

MASS (m/z) : 440 ( $M+1$ )Preparation 253IR (KBr) : 1778, 1599, 1576, 1527, 1498, 1473, 1439  $\text{cm}^{-1}$ NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.47 (3H, t,  $J=7.0\text{Hz}$ ), 4.11 (2H, q,15  $J=7.0\text{Hz}$ ), 7.02 (2H, d,  $J=8.9\text{Hz}$ ), 7.42-7.80 (7H, m),

8.10-8.56 (7H, m)

MASS (m/z) : 520 ( $M^++1$ )

The following compounds [Preparations 254 to 270] were  
obtained in a manner similar to that of Preparation 46.

20 Preparation 254IR (KBr) : 1702.2, 1702.8  $\text{cm}^{-1}$ NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 3.83 (3H, s), 8.06 (2H, d,  $J=8.7\text{Hz}$ ),8.20 (2H, d,  $J=8.7\text{Hz}$ ), 8.24 (1H, s), 9.31 (1H,

s), 10.04 (1H, s)

25 MASS (m/z) : 231 ( $M^++1$ )Preparation 255IR (KBr) : 1722, 1562, 1514, 1346, 1279  $\text{cm}^{-1}$ NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.90 (3H, s), 7.92 (2H, d,  $J=9.2\text{Hz}$ ),8.16 (1H, s), 8.38 (2H, d,  $J=9.2\text{Hz}$ ), 8.86 (1H, s)30 MASS (m/z) : 246 ( $M^++1$ )Preparation 256

IR (KBr) : 2937, 2856, 2819, 2213, 1608, 1517, 1448,

1384, 1349, 1247, 1224, 1180, 1122  $\text{cm}^{-1}$ NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.66 (6H, m), 3.32 (4H, t,  $J=5.0\text{Hz}$ ),35 6.83 (2H, d,  $J=9.1\text{Hz}$ ), 7.46 (2H, d,  $J=9.1\text{Hz}$ )

MASS (m/z) : 187 (M+H<sup>+</sup>)

Preparation 257

NMR (CDCl<sub>3</sub>, δ) : 3.28 (4H, t, J=4.9Hz), 3.85 (2H, d,  
J=4.9Hz), 6.87 (2H, d, J=9.0Hz), 7.52 (2H, d,  
J=9.0Hz)

MASS (m/z) : 189 (M+H<sup>+</sup>)

Preparation 258

NMR (CDCl<sub>3</sub>, δ) : 1.27 (6H, d, J=6.2Hz), 2.52 (2H, t,  
J=11.5Hz), 3.57 (2H, dd, J=2.2 and J=12.7Hz),  
3.6-3.9 (2H, m), 6.85 (2H, d, J=9.0Hz), 7.50 (2H,  
d, J=9.0Hz)

MASS (m/z) : 217 (M+H<sup>+</sup>)

Preparation 259

NMR (CDCl<sub>3</sub>, δ) : 2.69 (2H, t, J=5.1Hz), 3.77 (2H, t,  
J=5.1Hz), 6.81 (2H, d, J=9.0Hz), 7.49 (2H, d,  
J=9.0Hz)

MASS (m/z) : 205 (M+H<sup>+</sup>)

Preparation 260

NMR (CDCl<sub>3</sub>, δ) : 1.13 (3H, t, J=7.2Hz), 2.47 (2H, q,  
J=7.2Hz), 2.58 (4H, t, J=5.1Hz), 3.35 (4H, t,  
J=5.1Hz), 7.22 (2H, d, J=8.8Hz), 7.49 (2H, d,  
J=8.8Hz)

MASS (m/z) : 216 (M+H<sup>+</sup>)

Preparation 261

NMR (CDCl<sub>3</sub>, δ) : 1.36 (3H, t, J=7.1Hz), 1.55-1.75  
(2H, m), 1.80-2.10 (4H, m), 3.00-3.15 (2H, m),  
3.60-4.00 (3H, m), 4.31 (2H, q, J=7.1Hz), 6.82 (2H,  
d, J=9.1Hz), 7.90 (2H, d, J=9.1Hz)

APCI MASS (positive) : 250.3 (M<sup>+</sup>+1)

Preparation 262

NMR (CDCl<sub>3</sub>, δ) : 1.37 (3H, t, J=7.1Hz), 1.60-2.10  
(4H, m), 2.55-2.80 (1H, m), 2.95 (2H, dt, J=3.1Hz,  
J=12.3Hz), 3.90-4.05 (2H, m), 4.32 (2H, q, J=7.1Hz),  
6.90 (2H, d, J=9.1Hz), 7.10-7.35 (4H, m), 7.93 (2H,  
d, J=9.1Hz)

APCI MASS : 310.3 ( $M^+ + 1$ )

Preparation 263

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.29 (3H, t,  $J=7.1$ Hz), 3.21-3.34 (4H, m), 3.40-3.53 (4H, m), 4.24 (2H, q,  $J=7.1$ Hz), 6.81 (1H, t,  $J=7.2$ Hz), 7.00 (2H, d,  $J=7.9$ Hz), 7.05 (2H, d,  $J=9.0$ Hz), 7.25 (2H, t,  $J=7.9$ Hz), 7.81 (2H, d,  $J=8.9$ Hz)

MASS (m/z) : 311 ( $M^+ + 1$ )

Preparation 264

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.28 (3H, t,  $J=7.1$ Hz), 1.26-1.54 (2H, m), 1.64-1.90 (2H, m), 2.90-3.16 (2H, m), 3.58-3.84 (3H, m), 4.23 (2H, q,  $J=7.1$ Hz), 4.75 (1H, brs), 6.95 (2H, d,  $J=9.1$ Hz), 7.76 (2H, d,  $J=9.0$ Hz)

MASS (m/z) : 250 ( $M^+ + 1$ )

15 Preparation 265

IR (KBr) : 2939, 2843, 1703, 1601, 1552, 1497, 1439, 1414  $\text{cm}^{-1}$

20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.59 (2H, m), 1.87 (2H, m), 2.78-3.15 (3H, m), 3.79 (3H, s), 4.62 (2H, m), 6.92 (1H, d,  $J=9.1$ Hz), 7.21 (5H, m), 7.94 (1H, dd,  $J=9.1$  and 2.3Hz), 8.65 (1H, d,  $J=2.3$ Hz)

MASS (m/z) : 297 ( $M^+ + 1$ )

Preparation 266

25 IR (KBr) : 1707, 1610, 1516, 1444  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.04-1.30 (5H, m), 1.28 (3H, t,  $J=7.1$ Hz), 1.47-1.86 (5H, m), 2.16-2.34 (1H, m), 2.52-2.64 (4H, m), 3.19-3.34 (4H, m), 4.23 (2H, q,  $J=7.1$ Hz), 6.95 (2H, d,  $J=9.0$ Hz), 7.77 (2H, d,  $J=8.9$ Hz)

30 MASS (m/z) : 317 ( $M^+ + 1$ )

Preparation 267

35 IR (Nujol) : 1699, 1606  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.37 (3H, t,  $J=7.1$ Hz), 1.9-2.2 (4H, m), 3.01 (3H, s), 3.2-3.4 (2H, m), 3.6-3.8 (2H, m), 4.33 (2H, q,  $J=7.1$ Hz)

(+)APCI MASS : 374 (M+H)<sup>+</sup>

Preparation 268

IR (KBr) : 2927, 2850, 2212, 1602, 1517, 1442, 1394, 1253,  
1178, 1143, 927, 823 cm<sup>-1</sup>

5 NMR (CDCl<sub>3</sub>, δ) : 1.2 (5H, m), 1.65 (1H, m), 1.85 (4H, m),  
2.30 (1H, m), 2.70 (4H, t, J=5.1Hz), 3.32 (4H, t,  
J=5.1Hz), 6.85 (2H, d, J=9.0Hz), 7.48 (2H, d,  
J=9.0Hz)

MASS (m/z) : 270 (M+H<sup>+</sup>)

10 Preparation 269

Preparation 270

IR (KBr) : 1708.6, 1288.2, 1230.4 cm<sup>-1</sup>

15 NMR (CDCl<sub>3</sub>, δ) : 1.38 (3H, t, J=7.1Hz), 1.50-1.87 (6H,  
m), 3.34 (3H, s), 3.37-3.53 (10H, m), 4.00 (2H,  
t, J=6.4Hz), 4.34 (2H, q, J=7.1Hz), 6.90-7.04 (6H,  
m), 7.45-7.51 (4H, m), 7.94-7.98 (2H, m)

MASS (m/z) : 503 (M+1)

The following compounds [Preparations 271 to 279] were  
obtained in a manner similar to that of Preparation 16.

20 Preparation 271

IR (KBr) : 1724, 1558, 1521, 1257 cm<sup>-1</sup>

25 NMR (CDCl<sub>3</sub>, δ) : 0.91 (3H, t, J=6.9Hz), 1.3-1.9 (8H, m),  
3.87 (3H, s), 3.99 (2H, t, J=6.5Hz), 6.98 (2H, d,  
J=9.0Hz), 7.58 (2H, d, J=9.0Hz), 8.30 (1H, s), 8.53  
(1H, s)

MASS (m/z) : 303 (M<sup>+</sup>+1)

Preparation 272

30 NMR (CDCl<sub>3</sub>, δ) : 1.44 (3H, t, J=7.0Hz), 4.08 (2H, qt,  
J=7.0Hz), 6.98 (2H, d, J=8.8Hz), 7.56 (2H, d,  
J=8.8Hz), 7.62 (2H, d, J=8.6Hz), 8.07 (2H, d,  
J=8.6Hz)

MASS (m/z) : 257 (M<sup>+</sup>+1)

Preparation 273

35 IR (KBr) : 2947, 2875, 1722, 1603, 1527, 1495,  
1435 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.88-2.18 (4H, m), 3.51 (2H, m),  
3.93 (3H, s), 4.05 (2H, m), 6.98 (2H, d,  
J=8.6Hz), 7.50-7.70 (4H, m), 8.08 (2H, d, J=8.2Hz)

MASS (m/z) : 363 (M<sup>+</sup>+1), 365 (M<sup>+</sup>+3)

5     Preparation 274

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 3.40 (3H, s), 3.60 (2H, m), 3.73 (2H,  
m), 3.89 (2H, m), 3.93 (3H, s), 4.20 (2H, m), 7.01  
(2H, d, J=8.8Hz), 7.56 (2H, d, J=8.8Hz), 7.62 (2H,  
d, J=8.6Hz), 8.08 (2H, d, J=8.6Hz)

10     MASS (m/z) : 331 (M<sup>+</sup>+1)

Preparation 275

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.26 (3H, t, J=7.0Hz), 3.62 (2H, q,  
J=7.0Hz), 3.76-3.87 (2H, m), 3.93 (3H, s), 4.12-  
4.24 (2H, m), 6.96-7.08 (2H, m), 7.52-7.70 (4H, m),  
15     8.02-8.14 (2H, m)

MASS (m/z) : 301 (M<sup>+</sup>+1)

Preparation 276

IR (KBr) : 2949, 2877, 1722, 1695, 1603, 1529, 1497,  
1435 cm<sup>-1</sup>

20     NMR (CDCl<sub>3</sub>,  $\delta$ ) : 3.47 (3H, s), 3.78 (2H, m), 3.93  
(3H, s), 4.18 (2H, m), 6.95-7.08 (2H, m),  
7.48-7.68 (4H, m), 8.00-8.12 (2H, m)

MASS (m/z) : 287 (M<sup>+</sup>+1)

Preparation 277

25     IR (KBr) : 2954, 2873, 1718, 1610, 1544, 1494, 1471,  
1280, 1249, 1110 cm<sup>-1</sup>

MASS (m/z) : 408 ((M-TFA)+H<sup>+</sup>)

Preparation 278

30     IR (KBr) : 2935, 2867, 1720, 1610, 1544, 1494, 1471,  
1436, 1405, 1332, 1280, 1249, 1176, 1110 cm<sup>-1</sup>

MASS (m/z) : 436 (M+H<sup>+</sup>)

Preparation 279

35     IR (KBr) : 2950, 2867, 1708, 1608, 1525, 1471, 1409,  
1305, 1259, 1274, 1176, 1103 cm<sup>-1</sup>

MASS (m/z) : 450 (M+H<sup>+</sup>)



The following compounds [Preparations 280 to 309] were obtained in a manner similar to that of Preparation 47.

Preparation 280

IR (KBr) : 1653, 1626, 1574, 1524  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.85 (3H, m), 1.1-1.6 (10H, m), 3.44 (2H, t,  $J=6.4\text{Hz}$ ), 4.42 (2H, brs), 4.48 (2H, s), 7.44 (2H, d,  $J=8.6\text{Hz}$ ), 7.82 (2H, d,  $J=8.6\text{Hz}$ ), 8.12 (1H, s), 8.88 (1H, s), 9.48 (1H, brs)

MASS (m/z) : 331 ( $\text{M}^+ + 1$ )

10 Preparation 281

IR (KBr) : 1657, 1603, 1570, 1516, 1313  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 2.4-2.6 (4H, m), 3.0-3.2 (4H, m), 3.57 (2H, s), 4.41 (2H, d,  $J=4.3\text{Hz}$ ), 6.76 (1H, t,  $J=7.8\text{Hz}$ ), 6.92 (2H, d,  $J=7.8\text{Hz}$ ), 7.20 (2H, t,  $J=7.8\text{Hz}$ ), 7.47 (2H, t,  $J=8.5\text{Hz}$ ), 7.81 (2H, d,  $J=8.5\text{Hz}$ ), 8.12 (1H, s), 8.88 (1H, s), 9.48 (1H, t,  $J=4.3\text{Hz}$ )

MASS (m/z) : 377 ( $\text{M}^+ + 1$ )

Preparation 282

20 IR (KBr) : 1632, 1562, 1516  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.5-1.8 (6H, m), 3.0-3.3 (4H, m), 4.38 (2H, d,  $J=3.9\text{Hz}$ ), 7.03 (2H, d,  $J=9.1\text{Hz}$ ), 8.04 (1H, s), 8.70 (1H, s), 9.41 (1H, brs)

MASS (m/z) : 286 ( $\text{M}^+ + 1$ )

25 Preparation 283

IR (KBr) : 1649, 1623, 1522  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.8-1.0 (3H, m), 1.2-1.8 (8H, m), 4.00 (2H, t,  $J=4.0\text{Hz}$ ), 4.39 (2H, d,  $J=4.0\text{Hz}$ ), 7.05 (2H, d,  $J=9.0\text{Hz}$ ), 7.72 (2H, d,  $J=9.0\text{Hz}$ ), 8.07 (1H, s), 8.76 (1H, s), 9.44 (1H, t,  $J=4.0\text{Hz}$ )

MASS (m/z) : 303 ( $\text{M}^+ + 1$ )

Preparation 284

IR (KBr) : 1618, 1560, 1525  $\text{cm}^{-1}$

35 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.9-2.1 (4H, m), 3.1-3.3 (4H, m), 4.38 (2H, brs), 6.62 (2H, d,  $J=9.0\text{Hz}$ ), 7.58 (2H, d,

$J=9.0\text{Hz}$ ), 8.02 (1H, s), 8.64 (1H, s), 9.40 (1H, brs)

MASS (m/z) : 294 ( $M^+ + 23$ )

Preparation 285

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.10-1.40 (5H, m), 1.40-2.10 (10H, m),  
2.90-3.15 (2H, m), 3.25-3.50 (1H, m), 3.50-3.75 (3H,  
m), 4.05 (2H, d,  $J=3.9\text{Hz}$ ), 6.88 (2H, d,  $J=9.0\text{Hz}$ ),  
7.63 (2H, dd,  $J=9.0$  and  $2.0\text{Hz}$ )

APCI MASS (positive) : 318.3 ( $M^+ + 1$ )

Preparation 286

10 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.70-2.10 (4H, m), 2.60-2.85 (1H, m),  
2.85-3.05 (2H, m), 3.05-3.50 (2H, m), 3.85-4.10 (2H,  
m), 6.85-7.00 (2H, m), 7.10-7.40 (5H, m), 7.68 (2H,  
d,  $J=8.8\text{Hz}$ )

APCI MASS : 296 ( $M^+ + 1$ )

15 Preparation 287

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.20-2.10 (10H, m), 4.10 (2H, brs),  
4.20-4.40 (1H, m), 6.91 (2H, d,  $J=8.9\text{Hz}$ ), 7.49 (1H,  
brs), 7.78 (2H, d,  $J=8.9\text{Hz}$ )

ESI MASS : 257.3 ( $M^+ + \text{Na}$ )

20 Preparation 288

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.10-1.55 (5H, m), 1.60-2.00 (5H, m),  
2.40-2.65 (1H, m), 7.25 (2H, d,  $J=8.2\text{Hz}$ ), 7.67 (2H,  
d,  $J=8.2\text{Hz}$ )

APCI MASS : 219 ( $M^+ + 1$ )

25 Preparation 289

IR (KBr) : 2958, 2929, 2850, 2821, 1651, 1628, 1603, 1529,  
1487, 1443  $\text{cm}^{-1}$

30 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.00-1.36 (5H, m), 1.50-1.92 (5H, m),  
2.16-2.38 (1H, m), 2.57-2.64 (4H, m), 3.10-3.28 (4H,  
m), 4.48 (2H, s), 7.01 (2H, d,  $J=8.9\text{Hz}$ ), 7.59 (2H,  
d,  $J=8.8\text{Hz}$ ), 7.67 (2H, d,  $J=8.5\text{Hz}$ ), 7.86 (2H, d,  
 $J=8.4\text{Hz}$ ), 9.76 (1H, s)

MASS (m/z) : 379 ( $M^+ + 1$ )

Preparation 290

35 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 3.13-3.54 (8H, m), 4.38 (2H, s), 6.81

(1H, t, J=7.2Hz), 7.00 (2H, d, J=6.9Hz), 7.01 (2H, d, J=8.8Hz), 7.24 (2H, t, J=7.9Hz), 7.74 (2H, d, J=8.8Hz), 9.51 (1H, s)

MASS (m/z) : 297 (M<sup>+</sup>+1)

5 Preparation 291

NMR (DMSO-d<sub>6</sub>, δ) : 0.87 (3H, t, J=7.4Hz), 1.37-1.60 (4H, m), 1.80-1.98 (2H, m), 2.90-3.10 (2H, m), 3.38 (2H, t, J=6.6Hz), 3.38-3.70 (3H, m), 4.34 and 4.35 (2H, s), 6.92 (2H, d, J=9.0Hz), 7.68 (2H, d, J=8.9Hz),  
10 9.45 (1H, brs)

MASS (m/z) : 278 (M<sup>+</sup>+1)

Preparation 292

IR (KBr) : 1666, 1605, 1545, 1495, 1448 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.17 (6H, d, J=6.1Hz), 2.20-2.38 (2H, m), 3.59-3.78 (4H, m), 4.49 (2H, s), 7.03 (2H, d, J=8.9Hz), 7.61 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.5Hz), 7.87 (2H, d, J=8.4Hz), 9.77 (1H, -s)  
15

MASS (m/z) : 326 (M<sup>+</sup>+1)

Preparation 293

NMR (DMSO-d<sub>6</sub>, δ) : 0.88 (6H, s), 1.05-1.52 (6H, m), 1.52-1.73 (2H, m), 2.08-2.26 (1H, m), 2.52-2.72 (4H, m), 3.10-3.31 (4H, m), 4.36 (2H, s), 6.91 (2H, d, J=8.9Hz), 7.69 (2H, d, J=8.8Hz), 9.46 (1H, s)  
20

MASS (m/z) : 331 (M<sup>+</sup>+1)

25 Preparation 294

IR (KBr) : 1637, 1606, 1554, 1508, 1456 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.46-1.70 (2H, m), 1.87-2.06 (2H, m), 2.92-3.12 (2H, m), 3.52-3.73 (3H, m), 4.35 (2H, s), 4.54 (2H, s), 6.94 (2H, d, J=8.9Hz), 7.20-7.42 (5H, m), 7.69 (2H, d, J=8.8Hz), 9.45 (1H, s)  
30

MASS (m/z) : 326 (M<sup>+</sup>+1)

Preparation 295

NMR (DMSO-d<sub>6</sub>, δ) : 1.16-2.04 (10H, m), 4.29-4.51 (1H, m), 4.51 (2H, s), 7.03 (2H, d, J=8.8Hz), 7.64 (2H, d, J=8.8Hz), 7.69 (2H, d, J=8.4Hz), 7.88 (2H, d,  
35

$J=8.4\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 311 ( $M^+ + 1$ )

Preparation 296

IR (KBr) : 2912, 2870, 2846, 1608, 1597, 1533, 1493,  
5 1423  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.74 (2H, m), 1.97 (2H, m), 2.70-3.12  
(3H, m), 3.31 (2H, brs), 4.58 (2H, m), 6.69 (1H, d,  
 $J=9.0\text{Hz}$ ), 7.05-7.55 (6H, m), 7.88 (1H, dd,  $J=9.0$  and  
2.3Hz), 8.56 (1H, d,  $J=2.3\text{Hz}$ )

10 MASS (m/z) : 297 ( $M^+ + 1$ )

Preparation 297

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.35 (3H, t,  $J=7.0\text{Hz}$ ), 4.07 (2H, q,  
 $J=7.0\text{Hz}$ ), 4.50 (2H, s), 7.02 (2H, d,  $J=8.8\text{Hz}$ ),  
7.66 (2H, d,  $J=8.7\text{Hz}$ ), 7.70 (2H, d,  $J=8.4\text{Hz}$ ), 7.89  
15 (2H, d,  $J=8.4\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 257 ( $M^+ + 1$ )

Preparation 298

IR (KBr) : 2956, 2916, 2870, 1612, 1535, 1514,  
1493  $\text{cm}^{-1}$

20 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.55-1.87 (4H, m), 3.24 (3H, s),  
3.38 (2H, t,  $J=6.2\text{Hz}$ ), 4.03 (2H, t,  $J=6.1\text{Hz}$ ), 4.57  
(2H, brs), 7.03 (2H, d,  $J=8.7\text{Hz}$ ), 7.58-7.78 (4H,  
m), 7.89 (2H, d,  $J=8.3\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 315 ( $M^+ + 1$ )

25 Preparation 299

IR (KBr) : 1626, 1606, 1566, 1524, 1498, 1454  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.00-1.35 (5H, m), 1.35-1.90 (5H, m),  
2.16-2.36 (1H, m), 2.54-2.69 (4H, m), 3.12-3.28 (4H,  
m), 4.35 (2H, s), 6.91 (2H, d,  $J=8.9\text{Hz}$ ), 7.69 (2H,  
30 d,  $J=8.8\text{Hz}$ ), 9.46 (1H, s)

MASS (m/z) : 303 ( $M^+ + 1$ )

Preparation 300

IR (KBr) : 1659, 1626, 1606, 1531, 1498, 1446  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.89 (3H, d,  $J=6.8\text{Hz}$ ), 1.32-1.80  
35 (9H, m), 2.10-2.26 (1H, m), 2.50-2.65 (4H, m),

3.15-3.30 (4H, m), 4.36 (2H, s), 6.92 (2H, d, J=9.0Hz), 7.69 (2H, d, J=8.8Hz), 9.46 (1H, s)

MASS (m/z) : 317 ( $M^+ + 1$ )

Preparation 301

5 IR (KBr) : 1660, 1606, 1549, 1506, 1446  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, d, J=6.4Hz), 0.84-1.05 (2H, m), 1.05-1.54 (3H, m), 1.60-1.90 (4H, m), 2.12-2.33 (1H, m), 2.54-2.65 (4H, m), 3.11-3.27 (4H, m), 4.36 (2H, s), 6.91 (2H, d, J=8.9Hz), 7.69 (2H, d, J=8.8Hz),  
10 9.46 (1H, s)  
MASS (m/z) : 317 ( $M^+ + 1$ )

Preparation 302

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.17 (3H, t, J=7.0Hz), 3.51 (2H, q, J=7.0Hz), 4.50 (2H, m), 4.52 (2H, s), 7.42 (2H, d, J=8.2Hz),  
15 7.66-7.80 (4H, m), 7.92 (2H, d, J=8.9Hz), 9.83 (1H, s)  
MASS (m/z) : 271 ( $M^+ + 1$ )

Preparation 303

NMR (DMSO- $d_6$ ,  $\delta$ ) : 3.27 (3H, m), 3.45-3.68 (4H, m),  
20 4.54 (4H, s), 7.43 (2H, d, J=8.2Hz), 7.66-7.81 (4H, m), 7.92 (2H, d, J=8.4Hz), 9.83 (1H, s)  
MASS (m/z) : 301 ( $M^+ + 1$ )

Preparation 304

NMR (DMSO- $d_6$ ,  $\delta$ ) : 3.25 (3H, s), 3.44-3.55 (2H, m),  
25 3.55-3.65 (2H, m), 3.73-3.86 (2H, m), 4.08-4.20 (2H, m), 4.52 (2H, s), 7.05 (2H, d, J=8.8Hz), 7.67 (2H, d, J=8.7Hz), 7.70 (2H, d, J=8.4Hz), 7.89 (2H, d, J=8.5Hz), 9.80 (1H, s)  
MASS (m/z) : 331 ( $M^+ + 1$ )

30 Preparation 305

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.11 (3H, t, J=7.0Hz), 1.96 (2H, m),  
3.43 (2H, q, J=7.0Hz), 3.52 (2H, t, J=6.4Hz), 4.07 (2H, t, J=6.4Hz), 4.50 (2H, s), 7.03 (2H, d, J=8.8Hz),  
7.66 (2H, d, J=8.7Hz), 7.70 (2H, d, J=8.5Hz), 7.89 (2H, d, J=8.4Hz), 9.79 (1H, s)  
35

MASS (m/z) : 315 ( $M^+ + 1$ )

Preparation 306

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.14 (3H, t,  $J=7.0\text{Hz}$ ), 3.51 (2H, q,  $J=7.0\text{Hz}$ ), 3.66-3.80 (2H, m), 4.07-4.20 (2H, m), 4.51 (2H, s), 7.05 (2H, d,  $J=8.8\text{Hz}$ ), 7.67 (2H, d,  $J=8.8\text{Hz}$ ), 7.70 (2H, d,  $J=8.4\text{Hz}$ ), 7.89 (2H, d,  $J=8.4\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 301 ( $M^+ + 1$ )

Preparation 307

10 IR (KBr) : 2933, 2873, 1608, 1531, 1491  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.97 (2H, m), 3.26 (3H, s), 3.49 (2H, t,  $J=6.3\text{Hz}$ ), 4.07 (2H, t,  $J=6.4\text{Hz}$ ), 4.50 (2H, brs), 7.03 (2H, d,  $J=8.8\text{Hz}$ ), 7.66 (2H, d,  $J=8.7\text{Hz}$ ), 7.70 (2H, d,  $J=8.5\text{Hz}$ ), 7.88 (2H, d,  $J=8.4\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 301 ( $M^+ + 1$ )

Preparation 308

20 IR (KBr) : 2927, 2881, 1630, 1606, 1533, 1489  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 3.32 (3H, s), 3.67 (2H, m), 4.14 (3H, s), 4.52 (2H, s), 7.05 (2H, d,  $J=8.8\text{Hz}$ ), 7.67 (2H, d,  $J=8.8\text{Hz}$ ), 7.70 (2H, d,  $J=8.6\text{Hz}$ ), 7.89 (2H, d,  $J=8.4\text{Hz}$ ), 9.79 (1H, s)

MASS (m/z) : 287 ( $M^+ + 1$ )

Preparation 309

25 IR (Nujol) : 3292, 1603  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.8-2.2 (4H, m), 2.92 (3H, s), 3.0-3.2 (2H, m), 3.6-3.8 (2H, m), 4.36 (2H, s), 6.98 (2H, d,  $J=8.8\text{Hz}$ ), 7.44 (4H, s), 7.71 (2H, d,  $J=8.8\text{Hz}$ ), 9.46 (1H, s)

30 (+)APCI MASS : 360 ( $M+H$ ) $^+$

The following compounds [Preparations 310 to 345] were obtained in a manner similar to that of Preparation 7.

Preparation 310

35 IR (KBr) : 1724, 1282  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.9\text{Hz}$ ), 1.1-1.6 (10H,

m), 3.45 (2H, t, J=6.4Hz), 3.90 (3H, s), 4.50 (2H, s), 7.48 (2H, d, J=8.6Hz), 7.86 (2H, d, J=8.6Hz), 8.04 (2H, d, J=8.7Hz), 8.11 (2H, d, J=8.7Hz), 8.26 (1H, s), 9.02 (1H, s), 10.37 (1H, s), 10.70 (1H, s)

5        MASS (m/z) : 493 ( $M^+ + 1$ )

Preparation 311

IR (KBr) : 1718, 1614, 1279  $\text{cm}^{-1}$

10        NMR (DMSO- $d_6$ ,  $\delta$ ) : 2.4-2.6 (4H, m), 3.0-3.2 (4H, m),  
3.59 (2H, s), 3.90 (3H, s), 6.77 (1H, t, J=7.7Hz),  
6.92 (2H, d, J=7.7Hz), 7.20 (2H, t, J=7.7Hz), 7.50  
(2H, t, J=8.5Hz), 7.86 (2H, d, J=8.5Hz), 8.04 (2H,  
t, J=8.6Hz), 8.11 (2H, d, J=8.6Hz), 8.26 (1H, s),  
9.02 (1H, s), 10.37 (1H, s), 10.70 (1H, s)

MASS (m/z) : 539 ( $M^+ + 1$ )

15        Preparation 312

20        NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.10-2.00 (14H, m), 2.95-3.15 (2H, m),  
3.40-3.75 (4H, m), 3.90 (3H, s), 7.00 (2H, d,  
J=8.9Hz), 7.80 (2H, d, J=8.8Hz), 8.03 (2H, d,  
J=8.7Hz), 8.10 (2H, d, J=8.7Hz), 10.25 (1H, s),  
10.58 (1H, s)

APCI MASS (positive) : 480.3 ( $M^+ + 1$ )

Preparation 313

IR (KBr) : 1724, 1635, 1570, 1520, 1279  $\text{cm}^{-1}$

25        NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.5-1.7 (6H, m), 3.1-3.3 (4H, m),  
3.90 (3H, s), 7.05 (2H, d, J=9.1Hz), 7.66 (2H, d,  
J=9.1Hz), 8.04 (2H, d, J=8.7Hz), 8.11 (2H, d,  
J=8.7Hz), 8.85 (1H, s), 10.30 (1H, s), 10.68 (1H,  
s)

MASS (m/z) : 448 ( $M^+ + 1$ )

30        Preparation 314

IR (KBr) : 1716, 1603, 1552, 1521, 1470, 1284,  
1257  $\text{cm}^{-1}$

35        NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t, J=6.8Hz), 1.2-1.8 (8H,  
m), 3.90 (3H, s), 4.02 (2H, t, J=6.4Hz), 7.08 (2H,  
d, J=9.0Hz), 7.77 (2H, d, J=9.0Hz), 8.04 (2H, d,

J=8.7Hz), 8.11 (2H, d, J=8.7Hz), 8.91 (1H, s), 10.33 (1H, s), 10.69 (1H, s)

MASS (m/z) : 465 ( $M^+ + 1$ )

Preparation 315

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.60-1.95 (4H, m), 2.65-3.00 (3H, m), 3.90 (3H, s), 4.04 (2H, m), 7.05 (2H, d, J=8.9Hz), 7.10-7.40 (5H, m), 7.83 (2H, d, J=8.9Hz), 8.00-8.15 (4H, m), 10.27 (1H, s), 10.59 (1H, s)

APCI MASS : 458 ( $M^+$ )

10 Preparation 316

IR (KBr) : 1720, 1645, 1560, 1525, 1281  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.9-2.1 (4H, m), 3.2-3.4 (4H, m), 3.90 (3H, s), 6.64 (2H, d, J=9.0Hz), 7.63 (2H, d, J=9.0Hz), 8.04 (2H, d, J=8.7Hz), 8.11 (2H, d, J=8.7Hz), 8.15 (1H, s), 8.78 (1H, s), 10.28 (1H, s), 10.67 (1H, s)

MASS (m/z) : 456 ( $M^+ + 23$ )

Preparation 317

20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.10-2.10 (10H, m), 3.90 (3H, s), 4.35-4.55 (1H, m), 7.04 (2H, d, J=8.8Hz), 7.88 (2H, d, J=8.8Hz), 8.00-8.15 (4H, m), 10.41 (1H, s), 10.64 (1H, s)

APCI MASS (m/z) : 397 ( $M^+ + 1$ )

Preparation 318

25 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.15-1.60 (5H, m), 1.60-1.90 (5H, m), 2.50-2.70 (1H, m), 3.90 (3H, s), 7.37 (2H, d, J=8.3Hz), 7.85 (2H, d, J=8.2Hz), 8.00-8.15 (4H, m), 10.48 (1H, s), 10.68 (1H, s)

APCI MASS : 381 ( $M^+ + 1$ )

30 Preparation 319

IR (KBr) : 2927, 2852, 1722, 1684, 1645, 1603, 1495, 1446  $\text{cm}^{-1}$

35 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.00-1.36 (5H, m), 1.51-1.91 (5H, m), 2.20-2.38 (1H, m), 2.56-2.72 (4H, m), 3.12-3.28 (4H, m), 3.90 (3H, s), 7.03 (2H, d, J=8.9Hz), 7.64



(2H, d, J=8.7Hz), 7.77 (2H, d, J=8.5Hz), 7.97 (2H, d, J=8.4Hz), 8.00-8.16 (4H, m), 10.57 (1H, s), 10.71 (1H, s)

MASS (m/z) : 541 ( $M^+$ +1)

5 Preparation 320

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 3.21-3.54 (8H, m), 3.90 (3H, s), 6.82 (1H, t, J=7.2Hz), 7.01 (2H, d, J=7.9Hz), 7.08 (2H, d, J=8.9Hz), 7.25 (2H, t, J=7.9Hz), 7.85 (2H, d, J=8.8Hz), 8.04 (2H, d, J=8.6Hz), 8.09 (2H, d, J=8.6Hz), 10.31 (1H, s), 10.60 (1H, s)

MASS (m/z) : 459 ( $M^+$ +1)

Preparation 321

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.88 (3H, t, J=7.4Hz), 1.41-1.63 (4H, m), 1.84-2.01 (2H, m), 2.96-3.16 (2H, m), 3.40 (2H, t, J=6.6Hz), 3.40-3.76 (3H, m), 3.90 (3H, s), 7.00 (2H, d, J=8.9Hz), 7.80 (2H, d, J=8.8Hz), 8.00-8.16 (4H, m), 10.25 (1H, s), 10.58 (1H, s)

MASS (m/z) : 440 ( $M^+$ +1)

Preparation 322

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.18 (6H, d, J=6.1Hz), 2.18-2.43 (2H, m), 3.51-3.83 (4H, m), 3.90 (3H, s), 7.06 (2H, d, J=8.9Hz), 7.66 (2H, d, J=8.7Hz), 7.78 (2H, d, J=8.4Hz), 7.98 (2H, d, J=8.4Hz), 7.98-8.16 (4H, m), 10.58 (1H, s), 10.71 (1H, s)

MASS (m/z) : 488 ( $M^+$ +1)

Preparation 323

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.89 (6H, s), 1.05-1.72 (8H, m), 2.09-2.30 (1H, m), 2.54-2.73 (4H, m), 3.14-3.37 (4H, m), 3.90 (3H, s), 6.99 (2H, d, J=8.9Hz), 7.81 (2H, d, J=8.8Hz), 8.03 (2H, d, J=8.6Hz), 8.09 (2H, d, J=8.7Hz), 10.26 (1H, s), 10.58 (1H, s)

MASS (m/z) : 493 ( $M^+$ +1)

Preparation 324

IR (KBr) : 1714, 1687, 1653, 1605, 1560, 1522, 1460, 1439 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.45-1.70 (2H, m), 1.87-2.10 (2H, m),  
2.98-3.20 (2H, m), 3.56-3.78 (3H, m), 3.90 (3H, s),  
4.56 (2H, s), 7.01 (2H, d, J=9.0Hz), 7.21-7.46 (5H,  
m), 7.80 (2H, d, J=8.8Hz), 8.04 (2H, d, J=8.7Hz),  
5 8.09 (2H, d, J=8.7Hz), 10.26 (1H, s), 10.58 (1H, s)  
MASS (m/z) : 488 (M<sup>+</sup>+1)

Preparation 325

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.18-2.05 (10H, m), 3.90 (3H, s),  
4.34-4.50 (1H, m), 7.05 (2H, d, J=8.8Hz), 7.69 (2H,  
10 d, J=8.7Hz), 7.78 (2H, d, J=8.4Hz), 8.00 (2H, d,  
J=8.4Hz), 8.06 (2H, d, J=8.6Hz), 8.11 (2H, d,  
J=8.6Hz), 10.60 (1H, s), 10.72 (1H, s)  
MASS (m/z) : 473 (M<sup>+</sup>+1)

Preparation 326

15 IR (KBr) : 2945, 2852, 1720, 1693, 1645, 1601, 1524,  
1485 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.61 (2H, m), 1.87 (2H, m), 2.78-3.14  
(3H, m), 3.90 (3H, s), 4.61 (2H, m), 6.96 (1H, d,  
J=9.2Hz), 7.27 (5H, m), 7.98-8.10 (1H, m), 8.03 (2H,  
20 d, J=8.7Hz), 8.10 (2H, d, J=8.6Hz), 8.70 (1H, d,  
J=2.3Hz), 10.34 (1H, s), 10.62 (1H, s)  
MASS (m/z) : 459 (M<sup>+</sup>+1)

Preparation 327

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.36 (3H, t, J=7.0Hz), 3.90 (3H, s),  
25 4.09 (2H, q, J=6.9Hz), 7.04 (2H, d, J=8.8Hz), 7.71  
(2H, d, J=8.8Hz), 7.79 (2H, d, J=8.4Hz), 8.00 (2H,  
d, J=8.5Hz), 8.06 (2H, d, J=8.8Hz), 8.10 (2H, d,  
J=8.7Hz), 10.60 (1H, s), 10.72 (1H, s)  
MASS (m/z) : 419 (M<sup>+</sup>+1)

30 Preparation 328

IR (KBr) : 2951, 2872, 1724, 1680, 1651, 1605, 1554, 1497,  
1439 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.57-1.89 (4H, m), 3.25 (3H, s), 3.39  
(2H, t, J=6.2Hz), 3.91 (3H, s), 4.05 (2H, t, J=6.1Hz),  
35 7.05 (2H, d, J=8.8Hz), 7.71 (2H, d, J=8.7Hz), 7.79

(2H, d, J=8.4Hz), 8.00 (2H, d, J=8.5Hz), 8.06 (2H, d, J=8.7Hz), 8.10 (2H, d, J=8.7Hz), 10.61 (1H, s), 10.73 (1H, s)

MASS (m/z) : 477 ( $M^+ + 1$ )

5 Preparation 329

IR (KBr) : 1720, 1678, 1643, 1608, 1564, 1525,  
1502  $\text{cm}^{-1}$

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96-1.36 (5H, m), 1.49-1.91 (5H, m),  
2.16-2.35 (1H, m), 2.52-2.75 (4H, m), 3.10-3.35 (4H, m), 3.90 (3H, s), 6.99 (2H, d, J=8.9Hz), 7.81 (2H, d, J=8.8Hz), 8.04 (2H, d, J=8.6Hz), 8.09 (2H, d, J=8.7Hz), 10.27 (1H, s), 10.59 (1H, s)

MASS (m/z) : 465 ( $M^+ + 1$ )

Preparation 330

15 IR (KBr) : 1722, 1676, 1641, 1608, 1500, 1446  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.90 (3H, d, J=6.8Hz), 1.30-1.85 (9H, m), 2.11-2.30 (1H, m), 2.63-2.69 (4H, m), 3.18-3.38 (4H, m), 3.90 (3H, s), 6.99 (2H, d, J=9.0Hz), 7.81 (2H, d, J=8.8Hz), 8.04 (2H, d, J=9.1Hz), 8.09 (2H, d, J=8.7Hz), 10.27 (1H, s), 10.58 (1H, s)

20 MASS (m/z) : 479 ( $M^+ + 1$ )

Preparation 331

25 IR (KBr) : 1722, 1678, 1643, 1608, 1500, 1446  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, d, J=6.4Hz), 0.88-1.08 (2H, m), 1.08-1.51 (3H, m), 1.60-1.90 (4H, m), 2.14-2.35 (1H, m), 2.54-2.66 (4H, m), 3.13-3.36 (4H, m), 3.90 (3H, s), 6.98 (2H, d, J=8.9Hz), 7.81 (2H, d, J=8.8Hz), 8.03 (2H, d, J=8.7Hz), 8.09 (2H, d, J=8.6Hz), 10.26 (1H, s), 10.58 (1H, s)

30 MASS (m/z) : 479 ( $M^+ + 1$ )

Preparation 332

35 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.18 (3H, t, J=7.0Hz), 3.52 (2H, q, J=7.0Hz), 3.90 (3H, m), 4.52 (2H, s), 7.45 (2H, d, J=8.2Hz), 7.75 (2H, d, J=8.2Hz), 7.84 (2H, d, J=8.4Hz), 8.03 (2H, d, J=8.4Hz), 8.00-8.17 (4H, m),

10.64 (1H, s), 10.74 (1H, s)

MASS (m/z) : 433 ( $M^+ + 1$ )

Preparation 333

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 3.28 (3H, m), 3.47-3.66 (4H, m), 3.91  
(3H, s), 4.56 (2H, s), 7.46 (2H, d,  $J=8.3\text{Hz}$ ), 7.76  
(2H, d,  $J=8.2\text{Hz}$ ), 7.85 (2H, d,  $J=8.4\text{Hz}$ ), 7.98-8.16  
(6H, m), 10.65 (1H, s), 10.74 (1H, s)

MASS (m/z) : 463 ( $M^+ + 1$ )

Preparation 334

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 3.26 (3H, s), 3.39-3.55 (2H, m),  
3.55-3.66 (2H, m), 3.77 (2H, t,  $J=4.5\text{Hz}$ ), 3.90 (3H,  
s), 4.16 (2H, t,  $J=4.5\text{Hz}$ ), 7.08 (2H, d,  $J=8.8\text{Hz}$ ),  
7.72 (2H, d,  $J=8.8\text{Hz}$ ), 7.80 (2H, d,  $J=8.4\text{Hz}$ ), 8.00  
15 (2H, d,  $J=8.5\text{Hz}$ ), 8.06 (2H, d,  $J=8.7\text{Hz}$ ), 8.10 (2H,  
d,  $J=8.7\text{Hz}$ ), 10.61 (1H, s), 10.73 (1H, s)

MASS (m/z) : 493 ( $M^+ + 1$ )

Preparation 335

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.12 (3H, t,  $J=7.0\text{Hz}$ ), 1.88-2.12 (2H,  
m), 3.44 (2H, q,  $J=7.0\text{Hz}$ ), 3.53 (2H, t,  $J=6.4\text{Hz}$ ),  
20 3.91 (3H, s), 4.09 (2H, t,  $J=6.4\text{Hz}$ ), 7.06 (2H, d,  
 $J=8.8\text{Hz}$ ), 7.71 (2H, d,  $J=8.8\text{Hz}$ ), 7.79 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.00 (2H, d,  $J=8.5\text{Hz}$ ), 8.06 (2H, d,  
 $J=8.7\text{Hz}$ ), 8.10 (2H, d,  $J=8.7\text{Hz}$ ), 10.61 (1H, s),  
10.72 (1H, s)

25 MASS (m/z) : 477 ( $M^+ + 1$ )

Preparation 336

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.14 (3H, t,  $J=7.0\text{Hz}$ ), 3.52 (2H, q,  
 $J=7.0\text{Hz}$ ), 3.68-3.78 (2H, m), 3.90 (3H, s), 4.14-  
4.22 (2H, m), 7.08 (2H, d,  $J=8.8\text{Hz}$ ), 7.72 (2H, d,  
30  $J=8.8\text{Hz}$ ), 7.80 (2H, d,  $J=8.4\text{Hz}$ ), 8.00 (2H, d,  
 $J=8.4\text{Hz}$ ), 8.06 (2H, d,  $J=8.7\text{Hz}$ ), 8.10 (2H, d,  
 $J=8.7\text{Hz}$ ), 10.61 (1H, s), 10.73 (1H, s)

MASS (m/z) : 463 ( $M^+ + 1$ )

Preparation 337

35 IR (KBr) : 1724, 1680, 1655, 1605, 1495, 1437  $\text{cm}^{-1}$

NMR (DMSO-d<sub>6</sub>, δ) : 1.98 (2H, m), 3.26 (3H, s), 3.49 (2H, t, J=6.3Hz), 3.90 (3H, s), 4.09 (2H, t, J=6.4Hz), 7.06 (2H, d, J=8.8Hz), 7.71 (2H, d, J=8.8Hz), 7.79 (2H, d, J=8.5Hz), 8.00 (2H, d, J=8.5Hz), 8.06 (2H, d, J=8.7Hz), 8.10 (2H, d, J=8.7Hz), 10.60 (1H, s), 10.72 (1H, s)

MASS (m/z) : 463 (M<sup>+</sup>+1)

Preparation 338

IR (KBr) : 1724, 1682, 1645, 1605, 1495, 1439, 1404 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 3.33 (3H, s), 3.69 (2H, m), 3.90 (3H, s), 4.16 (2H, m), 7.07 (2H, d, J=8.9Hz), 7.72 (2H, d, J=8.7Hz), 7.72 (2H, d, J=8.7Hz), 7.80 (2H, d, J=8.6Hz), 9.79 (1H, s)

MASS (m/z) : 287 (M<sup>+</sup>+1)

Preparation 339

IR (Nujol) : 3259, 1724, 1672, 1626, 1605 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.9-2.2 (4H, m), 2.93 (3H, s), 3.0-3.4 (2H, m), 3.7-3.8 (2H, m), 3.90 (3H, s), 7.06 (2H, d, J=8.9Hz), 7.45 (4H, s), 7.82 (2H, d, J=8.9Hz), 8.0-8.2 (4H, m), 10.27 (1H, s), 10.59 (1H, s)

(+)APCI MASS : 522 (M+H)<sup>+</sup>

Preparation 340

IR (KBr) : 3247.5, 1727.9, 1687.4, 1255.4 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.23-1.99 (16H, m), 2.15-2.45 (2H, m), 3.21 (3H, s), 3.27-3.35 (2H, m), 3.60 (3H, s), 4.02 (2H, t, J=6.4Hz), 7.00 (2H, d, J=8.6Hz), 7.83 (2H, d, J=8.6Hz), 9.74 (1H, s), 10.12 (1H, s)

MASS (m/z) : 435 (M+1)

Preparation 341

IR (KBr) : 3236.0, 1724.0, 1677.8, 1255.4 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=7.0Hz), 1.30-1.50 (4H, m), 1.70-1.80 (2H, m), 3.87 (3H, s), 4.03 (2H, t, J=6.4Hz), 7.03-7.07 (2H, m), 7.68-8.00 (8H, m), 10.50-11.00 (2H, m)

MASS (m/z) : 467 (M+1)

Preparation 342

IR (KBr) : 3201.3, 1714.4, 1594.8, 1253.5  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.30-1.80 (8H, m), 2.42 (3H, s), 3.21  
5 (3H, s), 3.28-3.34 (2H, m), 3.34 (3H, s), 3.85 (3H,  
s), 4.04 (2H, t,  $J=6.4\text{Hz}$ ), 7.04 (2H, d,  $J=8.8\text{Hz}$ ),  
7.36 (1H, s), 7.73 (1H, s), 7.95 (2H, d,  $J=9\text{Hz}$ ), 10.22  
(1H, s), 10.39 (1H, s)

MASS (m/z) : 457 (M+1)

10 Preparation 343

IR (KBr) : 3199.3, 1716.3, 1608.3, 1253.5  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.37-1.80 (8H, m), 3.21 (3H, s),  
3.28-3.33 (2H, m), 3.71 (3H, s), 4.03 (2H, t,  
 $J=6.4\text{Hz}$ ), 6.39-6.59 (2H, m), 7.00-7.04 (2H, m),  
15 7.24-7.47 (2H, m), 7.83-7.88 (2H, m), 10.35 (2H, d,  
 $J=6.9\text{Hz}$ )

MASS (m/z) : 405 (M+1)

Preparation 344

IR (KBr) : 3193.5, 1718.3, 1606.4, 1249.6  $\text{cm}^{-1}$

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.00 (3H, t,  $J=7.4\text{Hz}$ ), 1.75-1.85 (2H,  
m), 3.97-4.03 (5H, m), 7.06-8.78 (12H, m), 10.64 (1H,  
s), 10.72 (1H, s)

MASS (m/z) : 483 (M+1)

Preparation 345

25 IR (KBr) : 3220.5, 1720.2, 1685.5, 1290.1,  
1251.6  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.30-1.80 (8H, m), 3.22 (3H, s),  
3.28-3.34 (2H, m), 3.94 (3H, s), 4.05 (2H, t,  
 $J=6.3\text{Hz}$ ), 7.04-7.08 (2H, m), 7.91-8.71 (8H, m),  
30 10.47 (1H, bs), 10.70 (1H, bs)

MASS (m/z) : 479 (M+1)

The following compounds [Preparations 346 to 355] were  
obtained in a manner similar to that of Preparation 41.

Preparation 346

35 IR (KBr) : 1726, 1284  $\text{cm}^{-1}$

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.89 (3H, t, J=6.8Hz), 1.2-1.8 (10H, m),  
3.51 (2H, t, J=6.6Hz), 3.97 (3H, s), 4.56 (2H, s),  
7.48 (2H, d, J=8.6Hz), 7.74 (2H, d, J=8.6Hz), 8.07  
(2H, d, J=8.6Hz), 8.17 (2H, d, J=8.6Hz), 8.18 (1H,  
s), 8.55 (1H, s)

MASS (m/z) : 491 (M<sup>+</sup>+1)

Preparation 347

NMR (CDCl<sub>3</sub>-CD<sub>3</sub>OD,  $\delta$ ) : 1.15-1.40 (6H, m), 1.40-2.30 (12H,  
m), 2.80-3.55 (4H, m), 3.65-3.80 (4H, m), 3.97 (3H,  
s), 4.00-4.25 (1H, m), 7.20 (2H, d, J=8.6Hz), 7.93  
(2H, d, J=8.6Hz), 8.06 (2H, d, J=8.6Hz), 8.16 (2H,  
d, J=8.6Hz)

ESI MASS (positive) : 478 (M<sup>+</sup>+1)

Preparation 348

NMR (CDCl<sub>3</sub>+CD<sub>3</sub>OD,  $\delta$ ) : 1.20-1.60 (5H, m), 1.65-2.05 (5H,  
m), 2.50-2.70 (1H, m), 3.97 (3H, s), 7.36 (2H, d,  
J=8.2Hz), 7.92 (2H, d, J=8.3Hz), 8.05-8.20 (4H, m)

APCI MASS (positive) : 379.2 (M<sup>+</sup>+1)

Preparation 349

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.20-2.15 (10H, m), 3.97 (3H, s),  
4.30-4.50 (1H, m), 7.01 (2H, d, J=8.9Hz), 7.92 (2H,  
d, J=8.9Hz), 8.00-8.30 (4H, m)

APCI MASS (positive) : 395.2 (M<sup>+</sup>+1)

Preparation 350

IR (KBr) : 1722, 1651, 1574, 1522, 1279 cm<sup>-1</sup>

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.92 (3H, t, J=6.7Hz), 1.2-1.9 (8H, m),  
3.97 (3H, s), 4.01 (2H, t, J=6.5Hz), 7.01 (2H, d,  
J=9.0Hz), 7.64 (2H, d, J=9.0Hz), 8.07 (2H, d,  
J=8.6Hz), 8.15 (1H, s), 8.17 (2H, d, J=8.6Hz), 8.46  
(1H, s)

MASS (m/z) : 465 (M<sup>+</sup>+1)

Preparation 351

IR (KBr) : 1727.9, 1249.6, 1180.2 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 1.30-2.30 (18H, m), 3.21 (3H, s),  
3.28-3.35 (2H, m), 3.62 (3H, s), 4.04 (2H, t,

J=6.4Hz), 7.07 (2H, d, J=8.7Hz), 7.85 (2H, d, J=8.7Hz)

MASS (m/z) : 433 (M+1)

Preparation 352

5 IR (KBr) : 1724.0, 1604.5, 1261.2, 1182.2 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 1.23-1.80 (8H, m), 2.48 (3H, s), 3.22 (3H, s), 3.22-3.33 (2H, m), 3.33 (3H, s), 3.87 (3H, s), 4.07 (2H, t, J=6.4Hz), 7.13 (2H, d, J=8.9Hz), 7.76-8.00 (4H, m)

10 MASS (m/z) : 455 (M+1)

Preparation 353

IR (KBr) : 1718.3, 1629.6, 1257.4, 1226.5 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 1.25-1.75 (8H, m), 3.21 (3H, s), 3.28-3.34 (2H, m), 3.72 (3H, s), 4.06 (2H, t, J=6.4Hz), 6.33-6.41 (2H, m), 7.09-7.13 (2H, m), 7.27-7.60 (2H, m), 7.90-7.95 (2H, m)

MASS (m/z) : 403 (M+1)

Preparation 354

IR (KBr) : 1716.3, 1297.9, 1255.4 cm<sup>-1</sup>  
20 NMR (DMSO-d<sub>6</sub>, δ) : 1.20-1.80 (8H, m), 3.22 (3H, s), 3.28-3.33 (2H, m), 3.95 (3H, s), 4.08 (2H, t, J=6.4Hz), 7.12-7.17 (2H, m), 7.97-8.73 (8H, m)  
MASS (m/z) : 477 (M+1)

Preparation 355

25 IR (KBr) : 2935.1, 2854.1, 1257.4, 827.3 cm<sup>-1</sup>  
NMR (CDCl<sub>3</sub>, δ) : 0.80-1.10 (3H, m), 1.20-1.60 (8H, m), 1.70-2.00 (2H, m), 4.01 (2H, t, J=6.5Hz), 6.96 (2H, d, J=8.8Hz), 7.44 (2H, d, J=8.7Hz), 7.54 (2H, d, J=8.7Hz), 7.89 (2H, d, J=8.8Hz), 7.95 (1H, s)

30 APCI MASS (m/z) : 430, 432

The following compounds [Preparations 356 to 382] were obtained in a manner similar to that of Preparation 48.

Preparation 356

IR (KBr) : 1714, 1514, 1277 cm<sup>-1</sup>  
35 NMR (CDCl<sub>3</sub>, δ) : 2.66 (4H, brs), 3.23 (4H, brs), 3.64 (2H,



s), 3.90 (3H, s), 6.92 (3H, m), 7.26 (2H, m), 7.52 (2H, d, J=8.0Hz), 7.73 (2H, d, J=8.0Hz), 8.0-8.3 (5H, m), 8.56 (1H, s)

MASS (m/z) : 537 ( $M^+ + 1$ )

5     Preparation 357

IR (KBr) : 1718, 1520, 1275, 1242  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.5-1.8 (6H, m), 3.24 (4H, t, J=5.3Hz), 3.97 (3H, s), 7.02 (2H, d, J=9.1Hz), 7.59 (2H, d, J=9.1Hz), 8.07 (2H, d, J=8.7Hz), 8.14 (1H, s), 8.17 (2H, d, J=8.7Hz), 8.44 (1H, s)

10

MASS (m/z) : 446 ( $M^+ + 1$ )

Preparation 358

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.50-1.95 (4H, m), 2.60-3.05 (3H, m), 3.90 (3H, s), 3.95-4.10 (2H, m), 6.90-7.35 (7H, m), 7.65-8.15 (6H, m)

15

APCI MASS (m/z) : 456 ( $M^+$ )

Preparation 359

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.0-2.2 (4H, m), 3.2-3.4 (4H, m), 3.97 (3H, s), 6.62 (2H, d, J=8.8Hz), 7.56 (2H, d, J=8.8Hz), 8.07 (2H, d, J=8.4Hz), 8.13 (1H, s), 8.17 (2H, d, J=8.4Hz), 8.40 (1H, s)

20

MASS (m/z) : 432 ( $M^+ + 1$ )

Preparation 360

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t, J=6.6Hz), 1.33-1.94 (6H, m), 3.99 (3H, s), 4.05 (2H, t, J=6.5Hz), 7.02 (2H, d, J=8.8Hz), 7.98 (2H, d, J=8.7Hz), 8.05-8.33 (8H, m)

25

MASS (m/z) : 543 ( $M^+ + 1$ )

Preparation 361

IR (KBr) : 1722, 1603, 1500, 1439, 1417  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.30-3.69 (8H, m), 3.93 (3H, s), 6.88-7.17 (3H, m), 7.03 (2H, d, J=9.0Hz), 7.34 (2H, t, J=7.7Hz), 7.94 (2H, d, J=8.8Hz), 8.08 (2H, d, J=8.6Hz), 8.16 (2H, d, J=8.6Hz)

30

35

MASS (m/z) : 457 ( $M^+ + 1$ )

Preparation 362

NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.95 (3H, t, J=7.4Hz), 1.40-2.16 (6H, m), 3.03-3.30 (2H, m), 3.45 (2H, t, J=6.7Hz), 3.44-3.95 (3H, m), 3.96 (3H, s), 6.85-7.12 (2H, m),  
5 7.80-7.97 (2H, m), 8.07 (2H, d, J=8.6Hz), 8.15 (2H, d, J=8.6Hz)

MASS (m/z) : 438 (M<sup>+</sup>+1)

Preparation 363

IR (KBr) : 1722, 1605, 1520, 1439, 1414 cm<sup>-1</sup>  
10 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 0.92 (6H, s), 1.12-1.90 (8H, m), 2.18-2.24 (1H, m), 2.68-2.86 (4H, m), 3.27-3.46 (4H, m), 3.96 (3H, s), 6.97 (2H, d, J=9.0Hz), 7.90 (2H, d, J=8.9Hz), 8.07 (2H, d, J=8.6Hz), 8.15 (2H, d, J=8.6Hz)

MASS (m/z) : 491 (M<sup>+</sup>+1)

15 Preparation 364

IR (KBr) : 1716, 1606, 1520, 1441, 1417 cm<sup>-1</sup>  
NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.70-2.26 (4H, m), 3.10-3.31 (2H, m), 3.60-3.84 (3H, m), 3.96 (3H, s), 4.60 (2H, s), 6.90-7.20 (2H, m), 7.26-7.46 (5H, m), 7.91 (2H, d, J=8.8Hz),  
20 J=8.8Hz), 8.09 (2H, d, J=8.7Hz), 8.15 (2H, d, J=8.7Hz)

MASS (m/z) : 486 (M<sup>+</sup>+1)

Preparation 365

IR (KBr) : 2941, 2845, 1713, 1601, 1549, 1504, 1431, 1404 cm<sup>-1</sup>  
25 NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.79 (2H, m), 2.01 (2H, m), 2.84 (1H, m), 3.08 (2H, m), 3.96 (3H, s), 4.64 (2H, m), 6.80 (1H, d, J=9.1Hz), 7.18-7.40 (5H, m), 8.03-8.23 (5H, m), 8.73 (1H, d, J=2.3Hz)

30 MASS (m/z) : 457 (M<sup>+</sup>+1)

Preparation 366

IR (KBr) : 2949, 2870, 1722, 1605, 1504, 1437 cm<sup>-1</sup>  
NMR (CDCl<sub>3</sub>,  $\delta$ ) : 1.66-2.00 (4H, m), 3.27 (3H, s), 3.47 (2H, t, J=6.0Hz), 3.97 (3H, s), 4.05 (2H, t, J=6.1Hz),  
35 7.00 (2H, d, J=8.6Hz), 7.59 (2H, d, J=8.6Hz), 7.70

(2H, d, J=8.2Hz), 8.00-8.14 (4H, m), 8.17 (2H, d, J=8.5Hz)

MASS (m/z) : 475 ( $M^+ + 1$ )

Preparation 367

5 IR (KBr) : 1720, 1605, 1522, 1439, 1416  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00-1.41 (5H, m), 1.56-2.14 (5H, m),  
2.24-2.41 (1H, m), 2.66-2.82 (4H, m), 3.27-3.43 (4H,  
m), 3.96 (3H, s), 6.96 (2H, d, J=9.0Hz), 7.89 (2H,  
d, J=8.9Hz), 8.06 (2H, d, J=8.6Hz), 8.14 (2H, d,  
10 J=8.6Hz)

MASS (m/z) : 463 ( $M^+ + 1$ )

Preparation 368

IR (KBr) : 1718, 1605, 1520, 1439, 1414  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, d, J=6.9Hz), 1.38-1.90 (9H,  
15 m), 2.24-2.47 (1H, m), 2.66-2.92 (4H, m), 3.28-3.53  
(4H, m), 3.96 (3H, s), 6.97 (2H, d, J=9.0Hz), 7.90  
(2H, d, J=8.9Hz), 8.07 (2H, d, J=8.7Hz), 8.15 (2H,  
d, J=8.7Hz)

MASS (m/z) : 477 ( $M^+ + 1$ )

20 Preparation 369

IR (KBr) : 1724, 1605, 1520, 1437, 1412  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.89 (3H, d, J=6.4Hz), 0.89-1.13 (2H,  
m), 1.13-2.07 (7H, m), 2.24-2.50 (1H, m), 2.68-2.93  
(4H, m), 3.30-3.52 (4H, m), 3.96 (3H, s), 6.97 (2H,  
25 d, J=8.9Hz), 7.90 (2H, d, J=8.9Hz), 8.07 (2H, d,  
J=8.6Hz), 8.15 (2H, d, J=8.6Hz)

MASS (m/z) : 477 ( $M^+ + 1$ )

Preparation 370

IR (KBr) : 2976, 1716, 1601, 1531, 1500, 1479,  
30 1437  $\text{cm}^{-1}$   
NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.46 (3H, t, J=7.0Hz), 3.97 (3H, s),  
4.10 (2H, q, J=7.0Hz), 7.00 (2H, d, J=8.7Hz), 7.59  
(2H, d, J=8.7Hz), 7.70 (2H, d, J=8.4Hz), 8.07 (2H,  
d, J=8.3Hz), 8.10-8.30 (4H, m)

35 MASS (m/z) : 417 ( $M^+ + 1$ )

Preparation 371

IR (KBr) : 2926, 2852, 1722, 1599, 1529, 1498,  
1437  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00-1.41 (5H, m), 1.51-2.05 (5H, m),  
2.24-2.43 (1H, m), 2.69-2.84 (4H, m), 3.22-3.36 (4H,  
m), 3.97 (3H, s), 7.02 (2H, d,  $J=8.8\text{Hz}$ ), 7.59 (2H,  
d,  $J=8.7\text{Hz}$ ), 7.70 (2H, d,  $J=8.4\text{Hz}$ ), 8.06 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.09-8.15 (4H, m)

MASS (m/z) : 539 ( $M^+ + 1$ )

10 Preparation 372

IR (KBr) : 1718, 1601, 1429  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.29 (6H, d,  $J=6.3\text{Hz}$ ), 2.36-2.56 (2H,  
m), 3.44-3.63 (2H, m), 3.74-3.93 (2H, m), 3.96 (3H,  
s), 6.99 (2H, d,  $J=8.9\text{Hz}$ ), 7.58 (2H, d,  $J=8.8\text{Hz}$ ),  
15 7.69 (2H, d,  $J=8.5\text{Hz}$ ), 8.05 (2H, d,  $J=8.4\text{Hz}$ ), 8.09  
(2H, d,  $J=8.6\text{Hz}$ ), 8.16 (2H, d,  $J=8.6\text{Hz}$ )

MASS (m/z) : 486 ( $M^+ + 1$ )

Preparation 373

IR (KBr) : 1707, 1603, 1529, 1498, 1433, 1414  $\text{cm}^{-1}$

20 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.23-2.12 (10H, m), 3.97 (3H, s),  
4.18-4.38 (1H, m), 7.00 (2H, d,  $J=8.8\text{Hz}$ ), 7.57 (2H,  
d,  $J=8.8\text{Hz}$ ), 7.69 (2H, d,  $J=8.4\text{Hz}$ ), 8.10 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.06-8.25 (4H, m)

MASS (m/z) : 471 ( $M^+ + 1$ )

25 Preparation 374

IR (KBr) : 2956, 2933, 2872, 1722, 1605, 1502,  
1435  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.00 (3H, t,  $J=7.2\text{Hz}$ ), 1.52 (2H, m), 1.79  
(2H, m), 3.97 (3H, s), 4.03 (2H, m), 7.00 (2H, m),  
30 7.45-7.78 (4H, m), 7.96-8.29 (6H, m)

MASS (m/z) : 445 ( $M^+ + 1$ )

Preparation 375

IR (KBr) : 1716, 1435  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.28 (3H, t,  $J=7.0\text{Hz}$ ), 3.60 (2H, q,  
35  $J=7.0\text{Hz}$ ), 3.97 (3H, m), 4.58 (2H, s), 7.47 (2H, d,

$J=8.3\text{Hz}$ ), 7.56-7.78 (4H, m), 8.04-8.29 (6H, m)

MASS (m/z) : 431 ( $M^+ + 1$ )

Preparation 376

IR (KBr) : 1720, 1651, 1606, 1560, 1504, 1435  $\text{cm}^{-1}$

5 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.42 (3H, m), 3.55-3.71 (4H, m), 3.97  
(3H, s), 4.64 (2H, s), 7.47 (2H, d,  $J=8.2\text{Hz}$ ), 7.64  
(2H, d,  $J=8.2\text{Hz}$ ), 7.68-7.80 (2H, m), 8.04-8.26 (6H,  
m)

MASS (m/z) : 461 ( $M^+ + 1$ )

10 Preparation 377

IR (KBr) : 2926, 2877, 1720, 1605, 1504, 1437  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.41 (3H, s), 3.54-3.64 (2H, m), 3.69-3.78  
(2H, m), 3.86-3.96 (2H, m), 3.97 (3H, s), 4.14-4.28  
(2H, m), 6.95-7.18 (2H, m), 7.51-5.64 (2H, m),  
15 5.64-6.77 (2H, m), 8.00-8.26 (6H, m)

MASS (m/z) : 491 ( $M^+ + 1$ )

Preparation 378

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.22 (3H, t,  $J=7.0\text{Hz}$ ), 2.09 (2H, m), 3.52  
(2H, q,  $J=7.0\text{Hz}$ ), 3.63 (2H, t,  $J=6.2\text{Hz}$ ), 3.97 (3H,  
20 s), 4.13 (2H, t,  $J=6.2\text{Hz}$ ), 7.02 (2H, d,  $J=8.8\text{Hz}$ ),  
7.59 (2H, d,  $J=8.8\text{Hz}$ ), 7.70 (2H, d,  $J=8.5\text{Hz}$ ), 8.07  
(2H, d,  $J=8.4\text{Hz}$ ), 8.08-8.26 (4H, m)

MASS (m/z) : 475 ( $M^+ + 1$ )

Preparation 379

25 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.27 (3H, t,  $J=7.0\text{Hz}$ ), 3.63 (2H, q,  
 $J=7.0\text{Hz}$ ), 3.74-3.90 (2H, m), 3.97 (3H, s), 4.14-  
4.28 (2H, m), 7.04 (2H, d,  $J=8.7\text{Hz}$ ), 7.59 (2H, d,  
 $J=8.7\text{Hz}$ ), 7.69 (2H, d,  $J=8.3\text{Hz}$ ), 8.06 (2H, d,  
 $J=8.2\text{Hz}$ ), 8.10 (2H, d,  $J=8.5\text{Hz}$ ),  
30 8.16 (2H, d,  $J=8.5\text{Hz}$ )

MASS (m/z) : 461 ( $M^+ + 1$ )

Preparation 380

IR (KBr) : 1722, 1605, 1531, 1500, 1435  $\text{cm}^{-1}$

35 NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 2.09 (2H, m), 3.38 (3H, s), 3.59 (2H,  
t,  $J=6.1\text{Hz}$ ), 3.97 (3H, s), 4.13 (2H, t,  $J=6.3\text{Hz}$ ),

7.02 (2H, d, J=8.8Hz), 7.50-7.64 (2H, m), 7.70 (2H, d, J=8.5Hz), 8.07 (2H, d, J=8.4Hz), 8.08-8.25 (4H, m)

MASS (m/z) : 461 ( $M^+ + 1$ )

5     Preparation 381

IR (KBr) : 1720, 1643, 1603, 1531, 1500, 1435  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 3.48 (3H, s), 3.80 (2H, m), 3.97 (3H, s), 4.18 (2H, m), 7.04 (2H, d, J=8.8Hz), 7.51-7.77 (4H, m), 8.03-8.23 (6H, m)

10     MASS (m/z) : 447 ( $M^+ + 1$ )

Preparation 382

IR (Nujol) : 1714, 1601  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.7-2.0 (4H, m), 2.75 (3H, s), 3.0-3.2 (2H, m), 3.4-3.6 (2H, m), 3.69 (3H, s), 6.77 (2H, d, J=8.8Hz), 7.08 (4H, s), 7.60 (2H, d, J=8.8Hz), 7.7-8.0 (4H, m)

15     (+)-APCI MASS : 520 ( $M + H$ )<sup>+</sup>

The following compounds [Preparations 383 to 388] were obtained in a manner similar to that of Preparation 33.

20     Preparation 383

IR (KBr) : 1699, 1684  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.86 (3H, t, J=6.6Hz), 1.2-1.7 (10H, m), 3.46 (2H, t, J=6.6Hz), 4.51 (2H, s), 7.50 (2H, d, J=8.6Hz), 7.95 (2H, d, J=8.6Hz), 8.13 (4H, s), 8.42 (1H, s), 9.36 (1H, s)

25     MASS (m/z) : 477 ( $M^+ + 1$ )

Preparation 384

IR (KBr) : 1583, 1543, 1516, 1396  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 2.4-2.6 (4H, m), 3.1-3.3 (4H, m), 3.60 (2H, s), 6.77 (1H, t, J=7.4Hz), 6.93 (2H, d, J=7.4Hz), 7.20 (2H, t, J=7.4Hz), 7.9-8.1 (6H, m), 8.39 (1H, s), 9.32 (1H, s)

30     MASS (m/z) : 523 ( $M^+ + 1$ )

Preparation 385

35     IR (KBr) : 1716, 1520, 1277, 1109  $\text{cm}^{-1}$

MASS (m/z) : 432 ( $M^+ + 1$ )

Preparation 386

IR (KBr) : 1684, 1518, 1252  $\text{cm}^{-1}$

Preparation 387

5 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.60-2.10 (4H, m), 2.70-3.10 (3H, m),  
4.08 (2H, m), 7.10-7.40 (7H, m), 7.95 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.18 (4H, AB-q,  $J=8.3\text{Hz}$ ,  $J=16.1\text{Hz}$ )

APCI MASS : 426 ( $M^+ + 1$ )

Preparation 388

10 IR (KBr) : 1687, 1610, 1568, 1527  $\text{cm}^{-1}$

MASS (m/z) : 418 ( $M^+ + 1$ )

The following compounds [Preparations 389 to 393] were  
obtained in a manner similar to that of Preparation 57.

Preparation 389

15 NMR ( $\text{CDCl}_3$ - $\text{CD}_3\text{OD}$ ,  $\delta$ ) : 2.10-2.25 (2H, m), 2.65-3.15 (3H,  
m), 3.45-3.70 (2H, m), 3.99 (3H, s), 7.30-7.40 (5H,  
m), 7.90-8.40 (8H, m) -

APCI MASS : 440 ( $M^+$ )

Preparation 390

20 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.10-2.10 (10H, m), 3.91 (3H, s),  
4.40-4.60 (1H, m), 7.17 (2H, d,  $J=8.9\text{Hz}$ ), 8.00-8.30  
(6H, m)

APCI MASS (positive) : 379.2 ( $M^+ + 1$ )

Preparation 391

25 NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.20-1.60 (5H, m), 1.60-1.95 (5H, m),  
2.50-2.75 (1H, m), 3.92 (3H, s), 7.50 (2H, d,  
 $J=8.3\text{Hz}$ ), 8.07 (2H, d,  $J=8.3\text{Hz}$ ), 8.18 (2H, d,  
 $J=8.7\text{Hz}$ ), 8.28 (2H, d,  $J=8.7\text{Hz}$ )

APCI MASS (positive) : 363.3 ( $M^+ + 1$ )

30 Preparation 392

IR (KBr) : 1724.0, 1253.5, 1199.5  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.0\text{Hz}$ ), 1.35-1.60 (4H,  
m), 1.70-1.95 (2H, m), 3.88-4.05 (5H, m), 6.98-7.03  
(2H, m), 7.57-8.17 (8H, m)

35 MASS (m/z) : 449 ( $M + 1$ )

Preparation 393

IR (KBr) : 1718.3, 1602.6, 1249.6  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.01 (3H, t,  $J=7.4\text{Hz}$ ), 1.50-1.80 (2H, m), 3.97-4.05 (5H, m), 7.06-7.10 (2H, m), 7.70-9.35 (12H, m)

MASS ( $m/z$ ) : 465 ( $M+1$ )

The following compounds [Preparations 394 to 457] were obtained in a manner similar to that of Preparation 49.

Preparation 394

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.10-1.95 (12H, m), 3.55-3.80 (4H, m), 7.08 (2H, d,  $J=8.9\text{Hz}$ ), 7.83 (2H, d,  $J=8.8\text{Hz}$ ), 8.07 (4H, s)

APCI MASS : 464 ( $M^+$ )

Preparation 395

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.10-1.60 (5H, m), 1.60-1.95 (5H, m), 2.50-2.70 (1H, m), 7.45 (2H, d,  $J=8.3\text{Hz}$ ), 7.96 (2H, d,  $J=8.3\text{Hz}$ ), 8.14 (4H, s)

Preparation 396

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.20-2.10 (10H, m), 4.35-4.60 (1H, m), 7.13 (2H, d,  $J=8.9\text{Hz}$ ), 7.95 (2H, d,  $J=8.9\text{Hz}$ ), 8.12 (4H, s)

APCI MASS (negative) : 379.2 ( $M^+-1$ )

Preparation 397

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.50-2.00 (4H, m), 2.65-3.10 (3H, m), 3.95-4.15 (2H, m), 6.90-7.35 (7H, m), 7.70-8.30 (6H, m)

APCI MASS : 442 ( $M^+$ )

Preparation 398

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.20-2.10 (10H, m), 4.40-4.60 (1H, m), 7.17 (2H, d,  $J=8.9\text{Hz}$ ), 7.95-8.30 (6H, m), 13.0-13.5 (1H, m)

APCI MASS (positive) : 365.2 ( $M^++1$ )

Preparation 399

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 1.15-1.60 (5H, m), 1.65-2.05 (5H, m), 2.50-2.70 (1H, m), 7.41 (2H, d,  $J=8.3\text{Hz}$ ), 8.05 (2H,



d,  $J=8.4\text{Hz}$ ), 8.23 (4H, s)

APCI MASS (positive) : 349.2 ( $M^+ + 1$ )

Preparation 400

IR (KBr) : 2935, 2858, 1705, 1649, 1601, 1531, 1500,  
1441, 1400  $\text{cm}^{-1}$

MASS ( $m/z$ ) : 523 ( $M^+ - 1$ )

Preparation 401

MASS ( $m/z$ ) : 527 ( $M^+ - 1$ )

Preparation 402

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 3.30-3.64 (8H, m), 6.75-7.33 (7H, m),  
7.70-8.29 (6H, m)

MASS ( $m/z$ ) : 443 ( $M^+ - 2\text{HCl} + 1$ )

Preparation 403

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=7.4\text{Hz}$ ),  
1.35-1.63 (4H, m), 1.82-2.03 (2H, m), 2.99-3.20  
(2H, m), 3.40 (2H, t,  $J=6.6\text{Hz}$ ), 3.40-3.80 (3H, m),  
7.09 (2H, d,  $J=9.0\text{Hz}$ ), 7.84 (2H, d,  $J=8.9\text{Hz}$ ), 8.11  
(4H, s), 13.22 (1H, brs)

MASS ( $m/z$ ) : 424 ( $M^+ - \text{HCl} + 1$ )

Preparation 404

IR (KBr) : 1686, 1601, 1531, 1500, 1421  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.18 (6H, d,  $J=6.1\text{Hz}$ ), 2.24-2.45 (2H,  
m), 3.63-3.82 (4H, m), 7.08 (2H, d,  $J=8.6\text{Hz}$ ), 7.68  
(2H, d,  $J=8.8\text{Hz}$ ), 7.90 (2H, d,  $J=8.5\text{Hz}$ ), 8.08 (2H,  
d,  $J=8.3\text{Hz}$ ), 8.13 (2H, d,  $J=8.7\text{Hz}$ ), 8.16 (2H, d,  
 $J=8.7\text{Hz}$ )

MASS ( $m/z$ ) : 472 ( $M^+ + 1$ )

Preparation 405

IR (KBr) : 1705, 1606, 1524, 1441, 1412  $\text{cm}^{-1}$

MASS ( $m/z$ ) : 477 ( $M^+ + 1$ )

Preparation 406

IR (KBr) : 1686, 1603, 1568, 1520, 1416  $\text{cm}^{-1}$

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 1.49-1.71 (2H, m), 1.90-2.10 (2H, m),  
3.06-3.24 (2H, m), 3.58-3.80 (3H, m), 4.56 (2H, s),  
7.10 (2H, d,  $J=9.0\text{Hz}$ ), 7.23-7.46 (5H, m), 7.85 (2H,

d,  $J=8.9\text{Hz}$ ), 8.10 (4H, m)

MASS (m/z) : 472 ( $M^+ + 1$ )

Preparation 407

IR (KBr) : 1682, 1606, 1572, 1524, 1498, 1427  $\text{cm}^{-1}$

5 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.25-2.05 (10H, m), 4.35-4.50 (1H, m),  
7.07 (2H, d,  $J=8.8\text{Hz}$ ), 7.64-7.94 (4H, m), 7.99-8.26  
(6H, m)

MASS (m/z) : 457 ( $M^+ + 1$ )

Preparation 408

10 IR (KBr) : 2933, 2846, 1686, 1599, 1552, 1500,  
1429  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.56-2.00 (4H, m), 2.74-3.18 (3H, m),  
4.62 (2H, m), 7.00-7.40 (6H, m), 7.99-8.26 (5H, m),  
8.74 (1H, s), 13.20 (1H, brs)

15 MASS (m/z) : 443 ( $M^+ + 1$ )

Preparation 409

IR (KBr) : 1686, 1603, 1574, 1527, 1500, 1427  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.36 (3H, t,  $J=7.0\text{Hz}$ ), 4.10 (2H, q,  
 $J=7.1\text{Hz}$ ), 7.00-7.13 (2H, m), 7.65-8.25 (10H, m)

20 MASS (m/z) : 403 ( $M^+ + 1$ )

Preparation 410

IR (KBr) : 1693, 1603, 1572, 1527, 1500, 1471,  
1425  $\text{cm}^{-1}$

25 NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.60-1.84 (4H, m), 3.25 (3H, s),  
3.30-3.50 (2H, m), 4.00-4.16 (2H, m), 7.07 (2H, d,  
 $J=8.8\text{Hz}$ ), 7.73 (2H, d,  $J=8.6\text{Hz}$ ), 7.87 (2H, d,  
 $J=8.5\text{Hz}$ ), 8.04-8.20 (6H, m)

MASS (m/z) : 461 ( $M^+ + 1$ )

Preparation 411

30 IR (KBr) : 1705, 1606, 1524, 1441, 1412  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.00-2.20 (10H, m), 3.00-3.35 (9H, m),  
7.18 (2H, d,  $J=9.1\text{Hz}$ ), 7.92 (2H, d,  $J=8.7\text{Hz}$ ), 8.11  
(4H, s)

MASS (m/z) : 447 ( $M^+ - 1$ )

Preparation 412

IR (KBr) : 1703, 1605, 1524, 1441, 1412  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.8\text{Hz}$ ), 1.43-2.00 (9H, m), 3.16-3.48 (9H, m), 7.17 (2H, d,  $J=8.4\text{Hz}$ ), 7.92 (2H, d,  $J=8.3\text{Hz}$ ), 8.12 (4H, s)

Preparation 413

IR (KBr) : 1705, 1605, 1524, 1443, 1414  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.88 (3H, d,  $J=6.4\text{Hz}$ ), 0.86-1.60 (5H, m), 1.74-1.92 (2H, m), 2.00-2.20 (2H, m), 2.97-3.35 (9H, m), 7.18 (2H, d,  $J=8.9\text{Hz}$ ), 7.92 (2H, d,  $J=8.8\text{Hz}$ ), 8.12 (4H, s)

Preparation 414

IR (KBr) : 2956, 2935, 2872, 1686, 1605, 1500, 1427  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.2\text{Hz}$ ), 1.44 (2H, m), 1.74 (2H, m), 4.05 (2H, m), 7.02-7.14 (2H, m), 7.66-8.30 (10H, m)

MASS (m/z) : 431 ( $M^+ + 1$ )

Preparation 415

IR (KBr) : 1686, 1606, 1425  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.18 (3H, t,  $J=7.0\text{Hz}$ ), 3.52 (2H, q,  $J=6.9\text{Hz}$ ), 4.53 (2H, s), 7.46 (2H, d,  $J=8.5\text{Hz}$ ), 7.77 (2H, d,  $J=8.3\text{Hz}$ ), 7.92 (2H, d,  $J=8.4\text{Hz}$ ), 8.10-8.24 (6H, m)

MASS (m/z) : 417 ( $M^+ + 1$ )

Preparation 416

IR (KBr) : 1682, 1605, 1566, 1425  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.28 (3H, m), 3.46-3.64 (4H, m), 4.56 (2H, s), 7.47 (2H, d,  $J=8.2\text{Hz}$ ), 7.78 (2H, d,  $J=8.2\text{Hz}$ ), 7.92 (2H, d,  $J=8.4\text{Hz}$ ), 8.07-8.25 (6H, m)

MASS (m/z) : 447 ( $M^+ + 1$ )

Preparation 417

IR (KBr) : 1684, 1603, 1500, 1423  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.26 (3H, s), 3.35-3.54 (2H, m),

3.54-3.68 (2H, m), 3.77 (2H, t,  $J=4.5\text{Hz}$ ), 4.17 (2H,

t, J=4.5Hz), 7.09 (2H, d, J=8.8Hz), 7.74 (2H, d, J=8.8Hz), 7.87 (2H, d, J=8.5Hz), 8.10 (2H, d, J=8.4Hz), 8.09-8.20 (4H, m)

MASS (m/z) : 477 ( $M^+ + 1$ )

5 Preparation 418

NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.12 (3H, t, J=7.0Hz), 1.97 (2H, m),  
3.39 (2H, q, J=7.0Hz), 3.53 (2H, t, J=6.3Hz), 4.09  
(2H, t, J=6.3Hz), 7.07 (2H, d, J=8.8Hz), 7.73 (2H,  
d, J=8.7Hz), 7.87 (2H, d, J=8.5Hz), 8.10 (2H, d,  
10 J=8.4Hz), 8.10-8.25 (4H, m)

Preparation 419

IR (KBr) : 1686, 1603, 1529, 1498, 1470, 1427  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.15 (3H, t, J=7.0Hz), 3.52 (2H, q,  
J=7.0Hz), 3.68-3.80 (2H, m), 4.13-4.24 (2H, m), 7.08  
15 (2H, d, J=8.8Hz), 7.73 (2H, d, J=8.8Hz), 7.86 (2H,  
d, J=8.5Hz), 8.09 (2H, d, J=8.4Hz), 8.10-8.21 (4H,  
m)

MASS (m/z) : 447 ( $M^+ + 1$ )

Preparation 420

IR (KBr) : 1686, 1603, 1529, 1498, 1470, 1427  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.98 (2H, m), 3.27 (3H, s),  
3.50 (2H, t, J=6.2Hz), 4.09 (2H, m), 7.07 (2H, d,  
J=8.8Hz), 7.73 (2H, d, J=8.8Hz), 7.87 (2H, d,  
J=8.5Hz), 8.10 (2H, d, J=8.5Hz), 8.10-8.21 (4H, m)

25 MASS (m/z) : 447 ( $M^+ + 1$ )

Preparation 421

IR (KBr) : 1684, 1603, 1525, 1500, 1421  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 3.32 (3H, s), 3.69 (2H, m), 4.17 (2H,  
m), 7.09 (2H, d, J=8.9Hz), 7.73 (2H, d, J=8.8Hz),  
30 7.87 (2H, d, J=8.6Hz), 8.03-8.20 (6H, m)

MASS (m/z) : 433 ( $M^+ + 1$ )

Preparation 422

IR (Nujol) : 1684, 1601  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.8-2.2 (4H, m), 2.94 (3H, s), 3.1-3.3  
35 (2H, m), 3.7-3.9 (2H, m), 7.14 (2H, d, J=8.9Hz), 7.45

(4H, s), 7.86 (2H, d, J=8.9Hz), 8.0-8.2 (4H, m)  
(+)APCI MASS : 506 (M+H)<sup>+</sup>

Preparation 423

IR (KBr) : 1664.3, 1602.6, 1230.4 cm<sup>-1</sup>

5 Preparation 424

IR (KBr) : 1685.5, 1608.3, 1238.1 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 2.79-4.42 (13H, m), 6.92-7.14 (2H, m),  
7.21-7.30 (4H, m), 7.81-7.96 (2H, m), 11.60 (1H, bs),  
12.55 (1H, bs)

10 MASS (m/z) : 323 (M+1)

Preparation 425

IR (KBr) : 1726.0, 1251.6, 1180.2 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.30-2.40 (18H, m), 3.21 (3H, s),  
3.28-3.35 (2H, m), 4.04 (2H, t, J=6.4Hz), 7.07 (2H,  
15 d, J=8.8Hz), 7.86 (2H, d, J=8.8Hz), 12.14 (1H, s)

MASS (m/z) : 419 (M+1)

Preparation 426

IR (KBr) : 1683.6, 1251.6, 825.4 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=6.9Hz), 1.24-1.55 (4H,  
20 m), 1.60-1.90 (2H, m), 4.00-4.10 (2H, m), 7.02-7.08  
(2H, m), 7.63-8.36 (8H, m)

MASS (m/z) : 435 (M+1)

Preparation 427

IR (KBr) : 1693.2, 1305.6, 1259.3, 1178.3 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 1.38-1.80 (8H, m), 2.56 (3H, s), 3.22  
(3H, s), 3.28-3.34 (5H, m), 4.06 (2H, t, J=6.4Hz),  
7.12 (2H, d, J=8.9Hz), 7.72 (1H, s), 7.86 (1H, s),  
7.97 (2H, d, J=8.8Hz), 13.12 (1H, bs)

MASS (m/z) : 441 (M+1)

30 Preparation 428

IR (KBr) : 1675.8, 1606.4, 1259.3 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 1.40-2.00 (8H, m), 3.35 (3H, s), 3.40  
(2H, t, J=6.3Hz), 4.03 (2H, t, J=6.3Hz), 6.13-6.20  
(2H, m), 6.96-7.94 (6H, m)

35 MASS (m/z) : 389 (M+1)

Preparation 429IR (KBr) : 1699.0, 1604.5, 1249.6, 1193.7  $\text{cm}^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.00 (3H, t,  $J=7.4\text{Hz}$ ), 1.67-1.85 (2H, m), 3.99 (2H, t,  $J=6.5\text{Hz}$ ), 7.04-7.09 (2H, m), 7.65-9.32 (12H, m)

MASS (m/z) : 451 (M+1)

Preparation 430IR (KBr) : 1685.5, 1253.5, 1174.4  $\text{cm}^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 1.20-1.80 (8H, m), 3.22 (3H, s), 3.29-3.35 (2H, m), 4.00-4.15 (2H, m), 7.12-7.17 (2H, m), 7.97-8.68 (8H, m)

MASS (m/z) : 463 (M+1)

Preparation 431

IR (KBr) : 2950.6, 1708.6, 1608.3, 1473.3, 1419.4,

1367.3, 1259.3, 1211.1, 1174.4  $\text{cm}^{-1}$ MASS (m/z) : 477 (M+H<sup>+</sup>)Preparation 432IR (KBr) : 2946, 1710, 1608, 1469, 1413, 1369, 1307, 1263, 1218, 1176  $\text{cm}^{-1}$ MASS (m/z) : 491 (M+H<sup>+</sup>)Preparation 433IR (KBr) : 2944, 1706, 1606, 1469, 1417, 1375, 1259, 1176  $\text{cm}^{-1}$ MASS (m/z) : 505 (M+H<sup>+</sup>)Preparation 434IR (KBr) : 3396, 2948, 2871, 1608, 1542, 1471, 1382, 1263, 1180, 1110  $\text{cm}^{-1}$ MASS (m/z) : 493 (M+H<sup>+</sup>)Preparation 435IR (KBr) : 2942, 1687, 1608, 1471, 1309, 1261, 1176  $\text{cm}^{-1}$ MASS (m/z) : 521 (M+H<sup>+</sup>)Preparation 436IR (KBr) : 2937, 1706, 1683, 1606, 1469, 1417, 1307, 1255, 1174, 1110  $\text{cm}^{-1}$

MASS (m/z) : 535 (M+H<sup>+</sup>)

Preparation 437

IR (KBr) : 2946, 2570, 1706, 1608, 1469, 1415, 1371,  
1309, 1259, 1216, 1174, 1108 cm<sup>-1</sup>

5 MASS (m/z) : 509 (M+H<sup>+</sup>)

Preparation 438

IR (KBr) : 2940, 2867, 2665, 2547, 1681, 1606, 1469, 1421,  
1311, 1290, 1255, 1176, 1116 cm<sup>-1</sup>

MASS (m/z) : 438 (M+H<sup>+</sup>)

10 Preparation 439

IR (KBr) : 2939, 2861, 1681, 1606, 1469, 1421, 1311, 1253,  
1174, 1114, 1016, 833 cm<sup>-1</sup>

MASS (m/z) : 452 (M+H<sup>+</sup>)

Preparation 440

15 IR (KBr) : 2935, 2858, 1681, 1606, 1571, 1467, 1419, 1311,  
1253, 1174, 1112 cm<sup>-1</sup>

MASS (m/z) : 466 (M+H<sup>+</sup>)

Preparation 441

IR (KBr) : 2931, 2854, 2663, 1679, 1606, 1467, 1421, 1311,  
20 1290, 1253, 1174, 1116 cm<sup>-1</sup>

MASS (m/z) : 480 (M+H<sup>+</sup>)

Preparation 442

IR (KBr) : 2935, 2850, 2819, 1608, 1589, 1537, 1473, 1417,  
25 1240 cm<sup>-1</sup>

MASS (m/z) : 405 (M+H<sup>+</sup>)

Preparation 443

IR (KBr) : 3361, 2969, 2848, 1606, 1585, 1535, 1475, 1402,  
1238, 1180, 1114, 927 cm<sup>-1</sup>

Preparation 444

30 IR (KBr) : 2975, 2873, 2829, 2665, 1681, 1606, 1469, 1423,  
1315, 1288, 1240, 1176 cm<sup>-1</sup>

MASS (m/z) : 435 (M+H<sup>+</sup>)

Preparation 445

IR (KBr) : 2969, 2530, 1672, 1604, 1467, 1423, 1288, 1267,  
35 1228, 1191 cm<sup>-1</sup>

MASS (m/z) : 423 (M+H<sup>+</sup>)

Preparation 446

IR (KBr) : 2937, 1702, 1606, 1473, 1405, 1369, 1268, 1241,  
1176 cm<sup>-1</sup>

5 MASS (m/z) : 434 (M+H<sup>+</sup>)

Preparation 447

MASS (m/z) : 488 (M+H<sup>+</sup>)

Preparation 448

10 IR (KBr) : 2956, 2869, 2665, 2543, 1681, 1608, 1544, 1492,  
1469, 1423, 1332, 1292, 1245, 1172 cm<sup>-1</sup>  
MASS (m/z) : 394 (M+H<sup>+</sup>)

Preparation 449

15 IR (KBr) : 2954, 2865, 2665, 2545, 1681, 1608, 1544, 1492,  
1423, 1332, 1292, 1247, 1172 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=6.8Hz), 1.3-1.5 (4H,  
m), 1.6-1.8 (2H, m), 4.00 (2H, t, J=6.8Hz), 6.99 (2H,  
d, J=8.8Hz), 7.82 (2H, d, J=8.8Hz), 8.11 (4H, s),  
8.69 (1H, s)  
MASS (m/z) : 408 (M+H<sup>+</sup>)

20 Preparation 450

IR (KBr) : 2933, 2865, 2667, 2545, 1681, 1608, 1544, 1492,  
1469, 1423, 1332 cm<sup>-1</sup>  
MASS (m/z) : 422 (M+H<sup>+</sup>)

Preparation 451

25 IR (KBr) : 2933, 2863, 1677, 1606, 1469, 1421, 1313, 1292,  
1255, 1174 cm<sup>-1</sup>  
MASS (m/z) : 422 (M+H<sup>+</sup>)

Preparation 452

30 IR (KBr) : 2935, 2871, 2667, 2545, 1683, 1608, 1542, 1525,  
1461, 1421, 1319, 1294, 1257, 1176 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=7.0Hz), 1.2-1.5 (4H,  
m), 1.6-1.9 (2H, m), 4.05 (2H, t, J=6.5Hz), 7.09 (2H,  
d, J=8.8Hz), 7.91 (2H, d, J=8.8Hz), 8.09 (2H, d,  
J=8.5Hz), 8.22 (2H, d, J=8.5Hz), 13.3 (1H, s)  
35 MASS (m/z) : 412 (M+H<sup>+</sup>)



Preparation 453IR (KBr) : 1726.0, 1687.4, 1259.3, 1176.4  $\text{cm}^{-1}$ NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 1.23-1.44 (4H, m), 1.85-1.96 (4H, m),  
2.10-2.40 (2H, m), 3.58 (3H, s), 12.08 (1H, s)

5        MASS (m/z) : 187 (M+1)

Preparation 454IR (KBr) : 1724.0, 1702.8, 1309.4, 1265.1  $\text{cm}^{-1}$ NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 2.49 (6H, s), 3.84 (3H, s), 7.70-7.72  
(2H, m), 13.14 (1H, bs)10        Preparation 455IR (KBr) : 1727.9, 1675.8, 1232.3  $\text{cm}^{-1}$ NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.70 (3H, s), 6.24-6.51 (2H, m),  
7.24-7.46 (2H, m), 12.66 (1H, bs)

MASS (m/z) : 157 (M+1)

15        Preparation 456IR (KBr) : 1726.0, 1685.5, 1286.3, 1251.6  $\text{cm}^{-1}$ NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.98 (3H, s), 7.68-7.77 (2H, m), 8.11  
(2H, s), 8.64-8.82 (2H, m), 13.58 (1H, bs)

MASS (m/z) : 231 (M+1)

20        Preparation 457IR (KBr) : 1724.0, 1697.1, 1290.1  $\text{cm}^{-1}$ NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 3.95 (3H, s), 8.04-8.08 (2H, m),  
8.20-8.27 (2H, m), 8.68-8.71 (2H, m)

MASS (m/z) : 231 (M+1)

25        Preparation 458

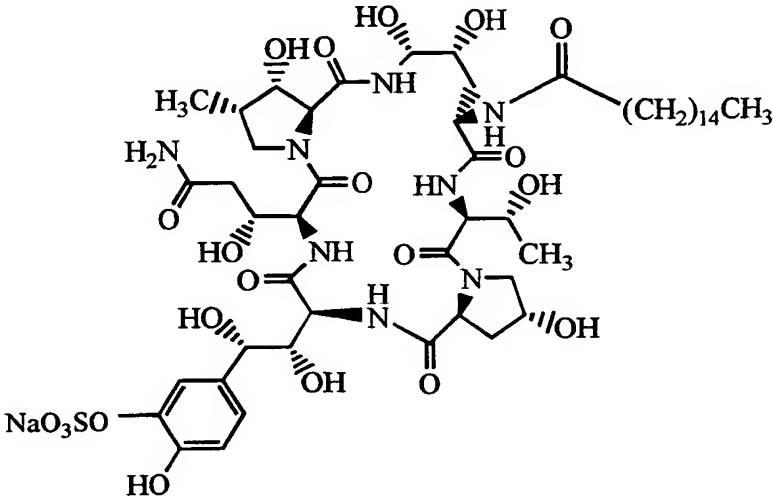
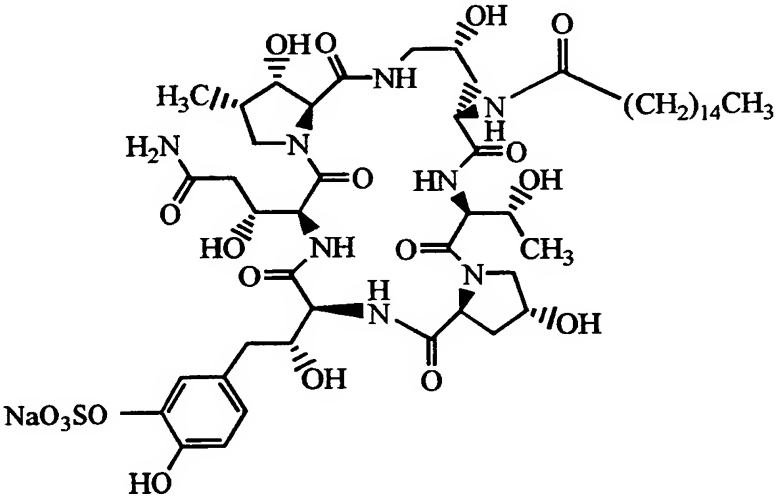
To a solution of 1-hydroxybenzotriazole (244 mg) and  
4-[5-(4-pentyloxyphenyl)isoxazol-3-yl]benzoic acid (528 mg)  
in dichloromethane (10 ml) was added 1-ethyl-3-(3'-  
dimethylaminopropyl)carbodiimide hydrochloride (WSCD·HCl)  
30 (430 mg) and the mixture was stirred for 4.5 hours at ambient  
temperature. The reaction mixture was added to water. The  
organic layer was taken and dried over magnesium sulfate.  
Magnesium sulfate was filtered off, and the filtrate was  
evaporated under reduced pressure to give 4-[5-(4-  
35 pentyloxyphenyl)isooxazol-3-yl]benzoic acid benzotriazol-

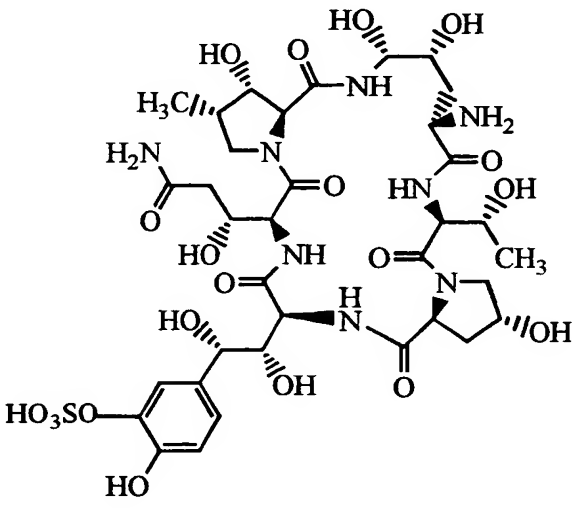
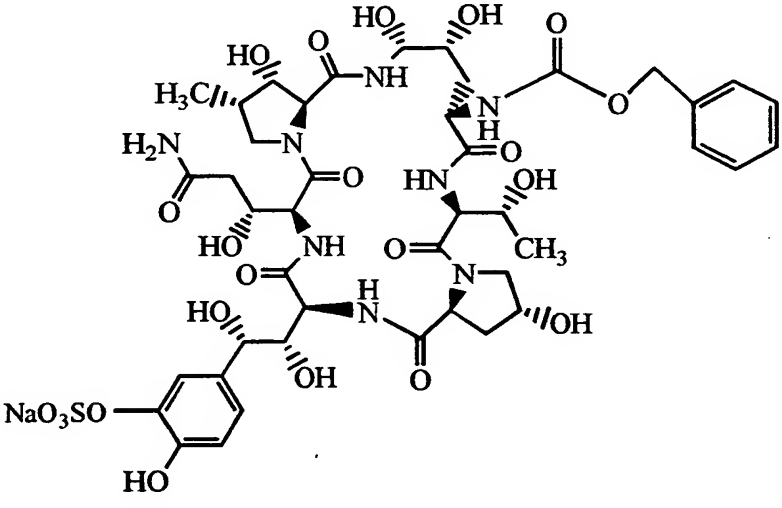
1-yl ester (640 mg).

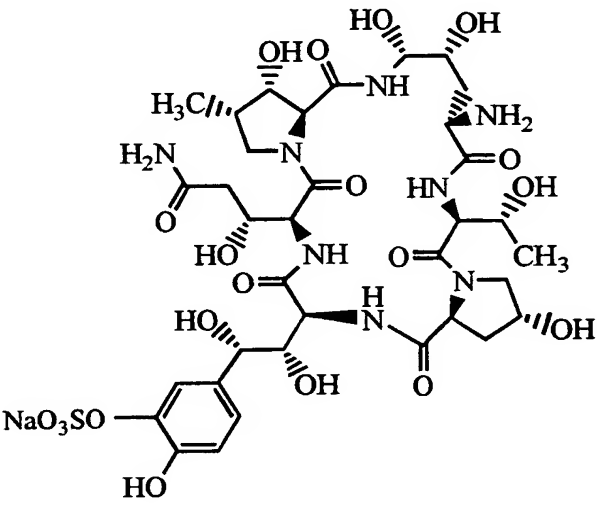
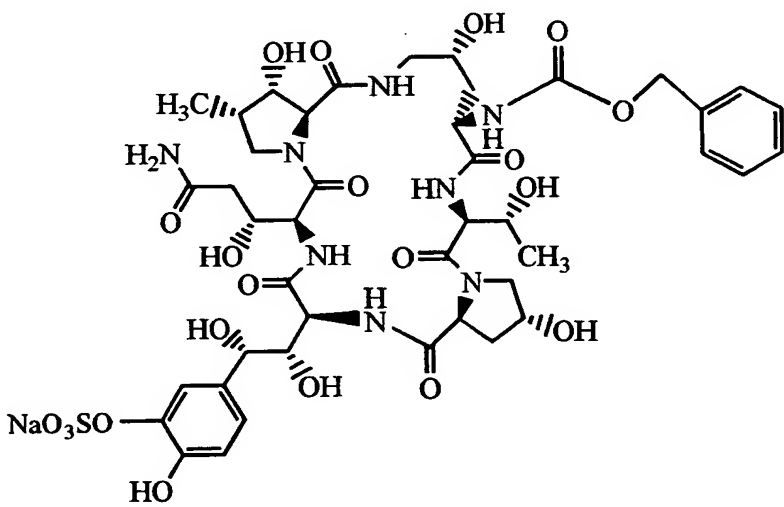
IR (KBr) : 1776.1, 1253.5, 1234.2, 1002.8  $\text{cm}^{-1}$

NMR ( $\text{CDCl}_3$ ,  $\delta$ ) : 0.95 (3H, t,  $J=7.0\text{Hz}$ ), 1.2-1.6 (4H, m), 1.6-1.9 (2H, m), 4.03 (2H, t,  $J=6.5\text{Hz}$ ), 6.81 (1H, s), 7.01 (2H, d,  $J=8.3\text{Hz}$ ), 7.3-7.6 (3H, m), 7.79 (2H, d,  $J=8.3\text{Hz}$ ), 8.11 (2H, d,  $J=8.0\text{Hz}$ ), 8.12 (1H, d,  $J=8.2\text{Hz}$ ), 8.39 (2H, d,  $J=8.0\text{Hz}$ )

The Starting Compounds (459) to (461) used and the Object Compounds (459) to (461) obtained in the following Preparations 459 to 461 are given in the table as below, in which the formula of the starting compounds are in the upper column and the formula of the object compounds are in the lower column, respectively.

Preparation No.	Formula
	
459	

Preparation No.	Formula
	
460	

Preparation No.	Formula
	 <p>The structure is a complex polycyclic molecule. It features a central core with several fused and linked rings. Key features include: a sodium sulfonate group (<math>\text{NaO}_3\text{SO}-</math>) attached to a phenyl ring; multiple hydroxyl groups (<math>\text{OH}</math>) at various stereocenters; amide bonds (<math>\text{NH}</math>, <math>\text{C=O}</math>); and a methyl group (<math>\text{CH}_3</math>) on a nitrogen-containing ring. Stereochemistry is indicated with wedges and dashes.</p>
461	 <p>This structure is similar to the one above but has a different substituent on the right-hand side. Instead of a hydroxyl group, it features a benzyl ester group (<math>-\text{C}(=\text{O})\text{OCH}_2\text{C}_6\text{H}_5</math>). The rest of the molecule, including the sodium sulfonate group, hydroxyl groups, amide bonds, and methyl group, remains the same.</p>

Preparation 459

To a suspension of Starting Compound (459) (5.0 g) and triethylsilane (6.67 ml) in dichloromethane (125 ml) was dropwise added trifluoroacetic acid (32.2 ml) with stirring under ice-cooling. The mixture was stirred at ambient temperature for 2 hours. The reaction mixture was slowly poured into pH6.86 standard buffer solution (1.2 L) with stirring under ice-cooling adjusting pH to 8.5-10 with 1N sodium hydroxide. The mixture was evaporated in vacuo to remove the organic solvent and chromatographed on nonionic adsorption resin, Diaion SP-205 (Trademark, prepared by Mitsubishi Chemical Industries) (400 ml) eluting in turn with water (2 L), 10% aqueous methanol (2 L), 20% aqueous methanol (2 L), 30% aqueous methanol (2 L), 50% aqueous methanol (2 L), 60% aqueous methanol (2 L) and 90% aqueous methanol (2 L). The fractions containing the desired compound were collected and evaporated in vacuo. The resulting residue was lyophilized to give Object Compound (459) (3.13 g).

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=7.0\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.02 (3H, d,  $J=6.1\text{Hz}$ ), 1.24 (26H, m), 1.35-1.50 (2H, m), 1.55-2.50 (11H, m), 2.80-3.30 (2H, m), 3.60-5.40 (20H, m), 6.60-6.80 (3H, m), 6.85-7.75 (5H, m), 8.00-8.15 (2H, m), 8.71 (1H, broad S)

APCI MASS (m/z) : 1141.1 ( $M^+-Na$ )

Preparation 460

A solution of Starting Compound (460) (100 g) in a mixture of tetrahydrofuran (1 L) and pH6.86 standard buffer solution (1 L) was dropwise added benzyloxycarbonyl chloride (16.8 ml) at 5-10°C adjusting pH to 7.0-8.0 with saturated aqueous sodium hydrogen carbonate. The solution was stirred at the same conditions for 3 hours and adjusted pH to 6.0 with 1N hydrochloride. The mixture was evaporated in vacuo to remove organic solvent. The residue was passed ion exchange resin, DOWEX 50WX4  $Na^+$  type (prepared by Dow Chemical) (1 L) and washed with water (3 L). The eluate was chromatographed on reversed

phase silica gel (ODS SP-120, prepared by Daiso Co., Ltd.) (2.5 L) with water (12 L), 10% aqueous methanol (12 L) and 20% aqueous methanol (12 L) successively. The fractions containing the object compound were collected, concentrated by evaporation in vacuo and lyophilized to give Object Compound (460) (76 g, yield 65%)

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.05 (3H, d,  $J=5.7\text{Hz}$ ), 1.60-2.50 (7H, m), 3.10-5.20 (29H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.75-6.90 (2H, m), 6.90-7.10 (2H, m), 7.20-7.40 (7H, m), 7.63 (1H, d,  $J=7.8\text{Hz}$ ), 8.00-8.15 (2H, m)

ESI MASS (Negative) : 1069.3 ( $M^+-Na$ )

#### Preparation 461

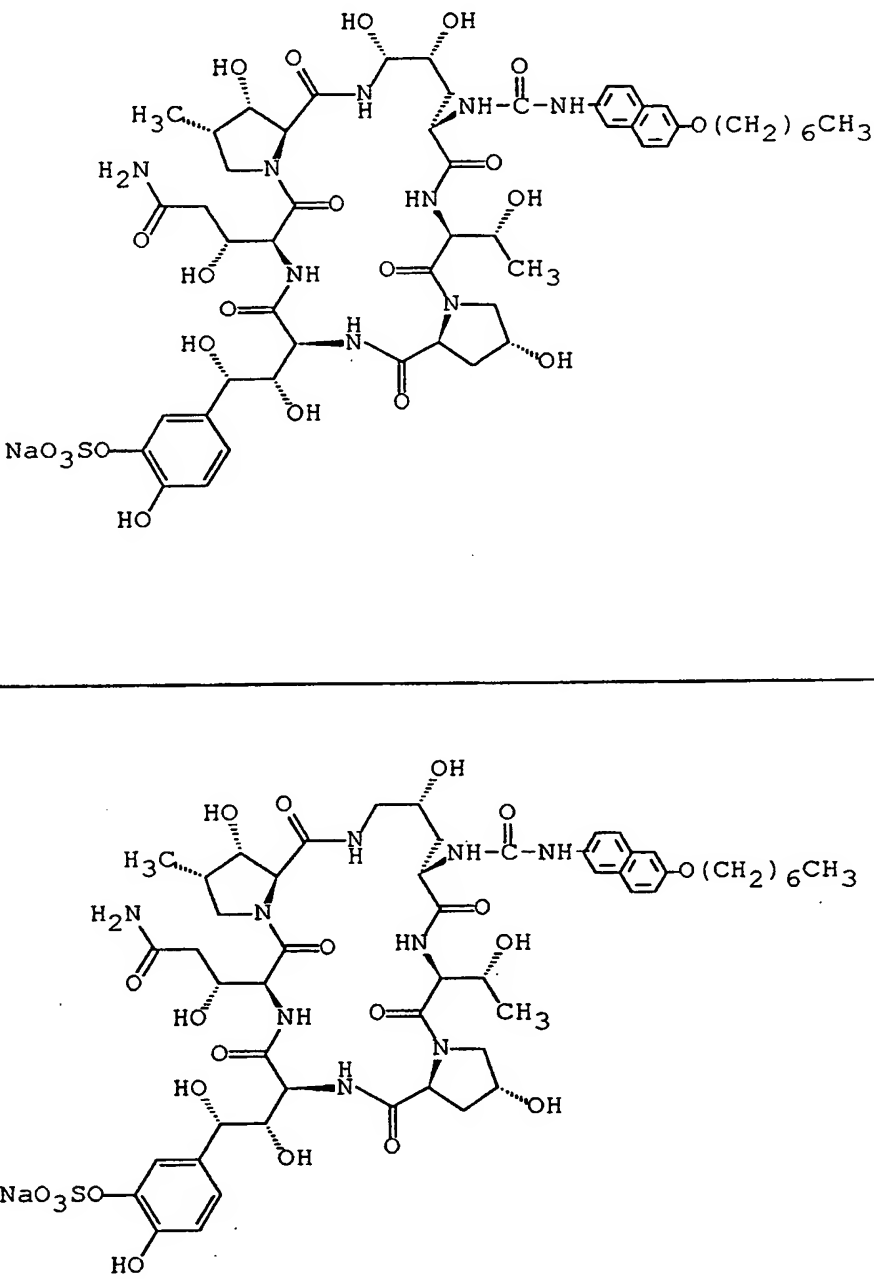
To a solution of Starting Compound (461) (30 g) and sodium cyanoborohydride (3.45 g) in dichloromethane (300 ml) was dropwise added trifluoroacetic acid (150 ml) with stirring under in ice-cooling. The mixture was stirred at the same condition for 3 hours. The reaction mixture was slowly poured into pH6.86 standard buffer solution (1.2 L) with stirring on ice-sodium chloride bath adjusting pH to 8.5-10 with 1N sodium hydroxide. An aqueous layer was separated and cooled at refrigerator overnight. The aqueous solution was evaporated in vacuo to remove organic solvent and chromatographed on reversed phase silica gel (ODS SP-120, prepared by Daiso Co., Ltd.) (700 ml) eluting with water (5 L) and 5% aqueous methanol (6 L) successively. The fractions containing the object compound were collected, concentrated by evaporation in vacuo and lyophilized to give Object Compound (461) (17.3 g)

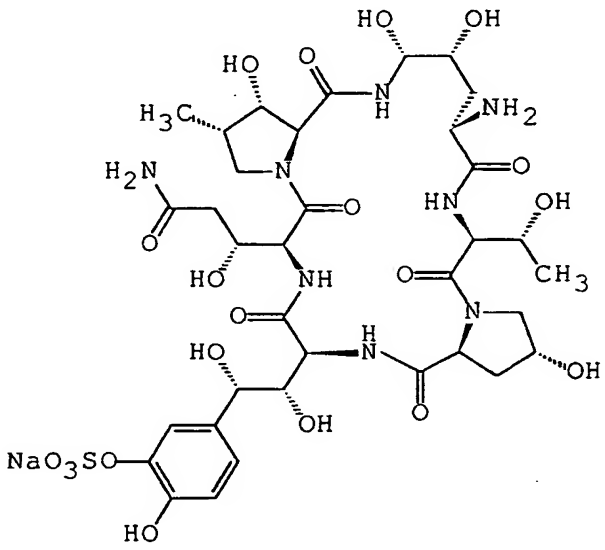
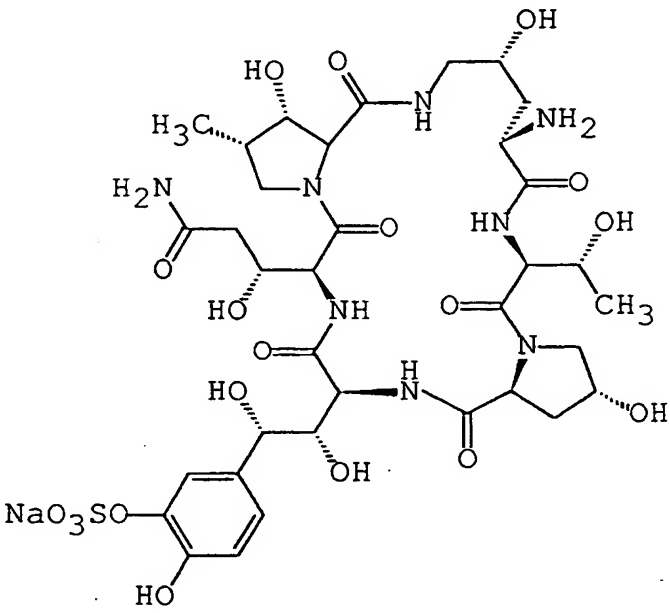
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.07 (3H, d,  $J=5.7\text{Hz}$ ), 1.40-2.45 (7H, m), 2.85-3.30 (2H, m), 3.60-4.50 (13H, m), 4.60-5.35 (10H, m), 6.65-7.10 (5H, m), 7.20-7.75 (8H, m), 7.92 (1H, broad d,  $J=8.4\text{Hz}$ ), 8.84 (1H, s)

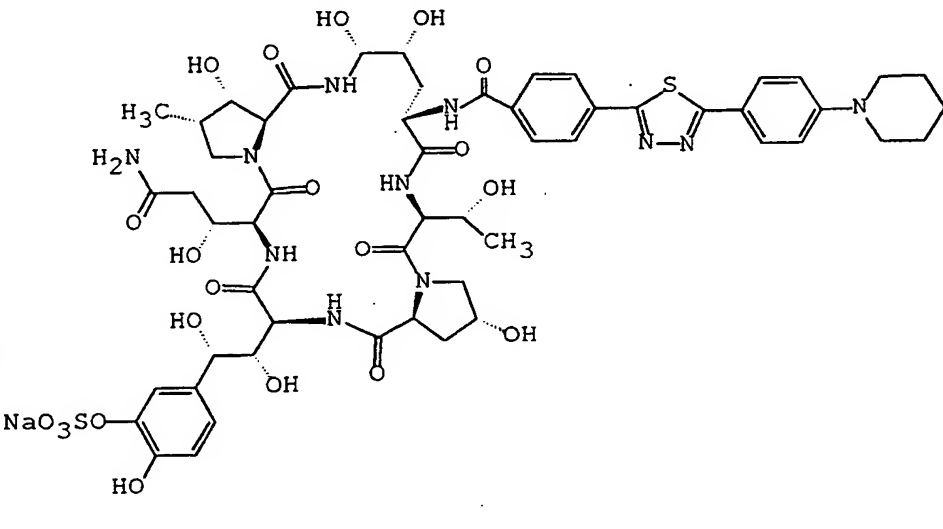
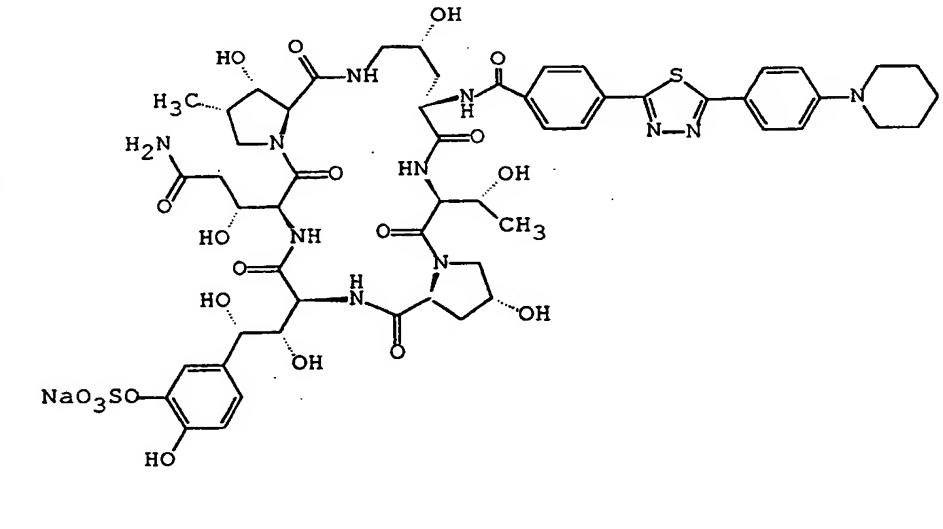
ESI MASS (Negative) : 1053.3 ( $M^+-Na$ )

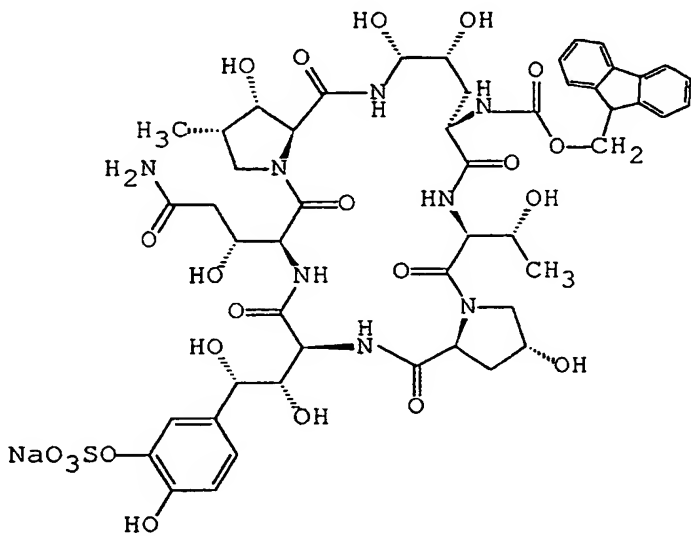
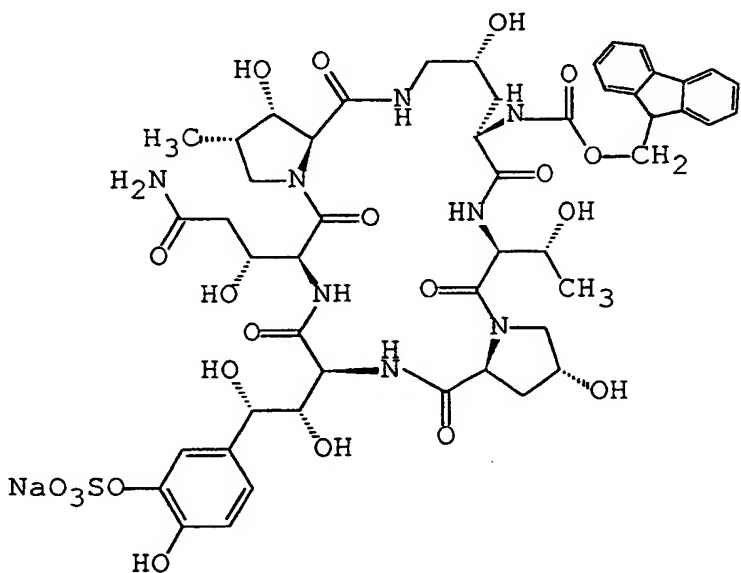
The Starting Compounds (1) to (169) used and the Object Compounds (1) to (169) obtained in the following Examples 1 to 169 are given in the table as below, in which the formulas of the starting compounds are in the upper column and the  
5 formulas of the object compounds are in the lower column, respectively.

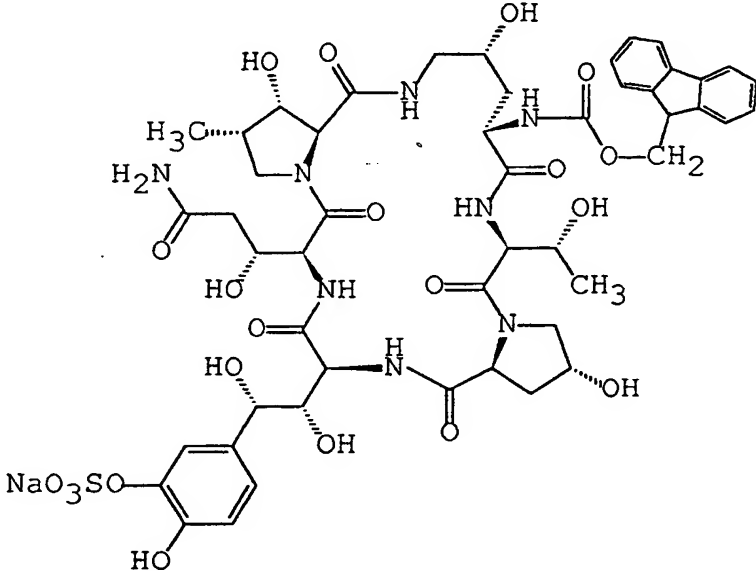
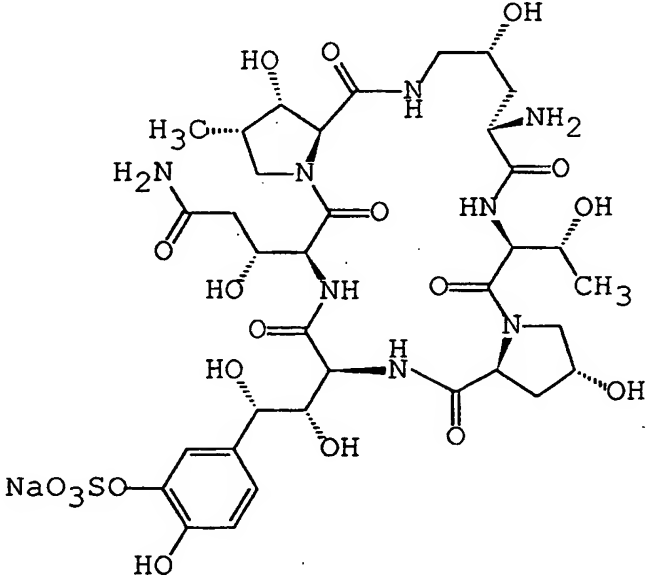


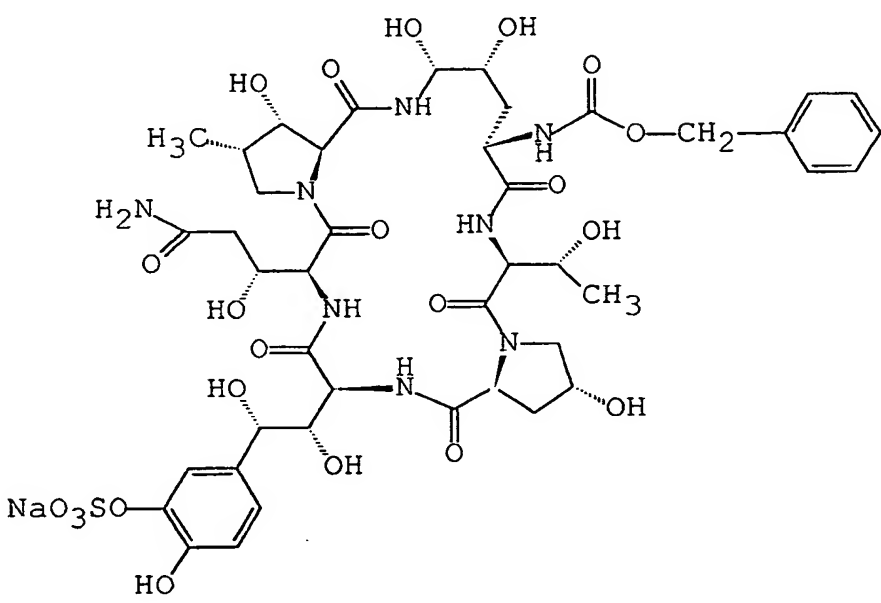
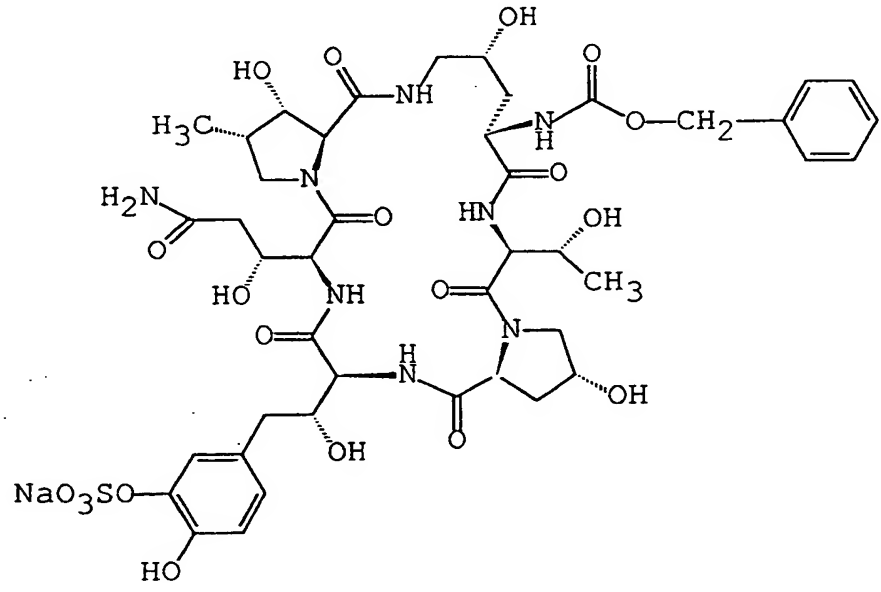
Example No.	Formula
1	 <p>The chemical structure is a complex molecule, likely a peptide derivative, featuring multiple amide bonds, hydroxyl groups, and a sodium sulfonate group. The structure is shown in two identical representations, one above the other. The molecule consists of a central core with various side chains, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The structure is highly symmetrical and complex, with many stereocenters indicated by wedges and dashes.</p>

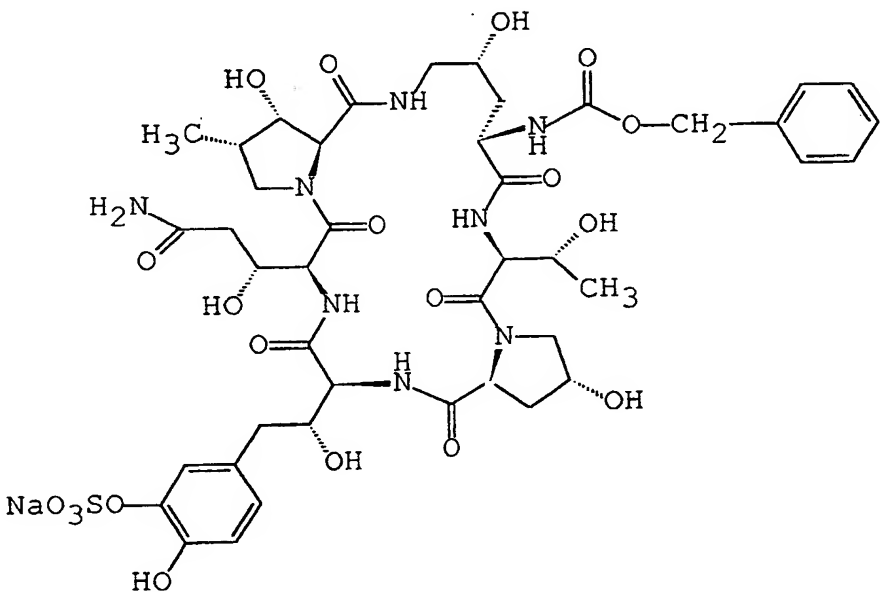
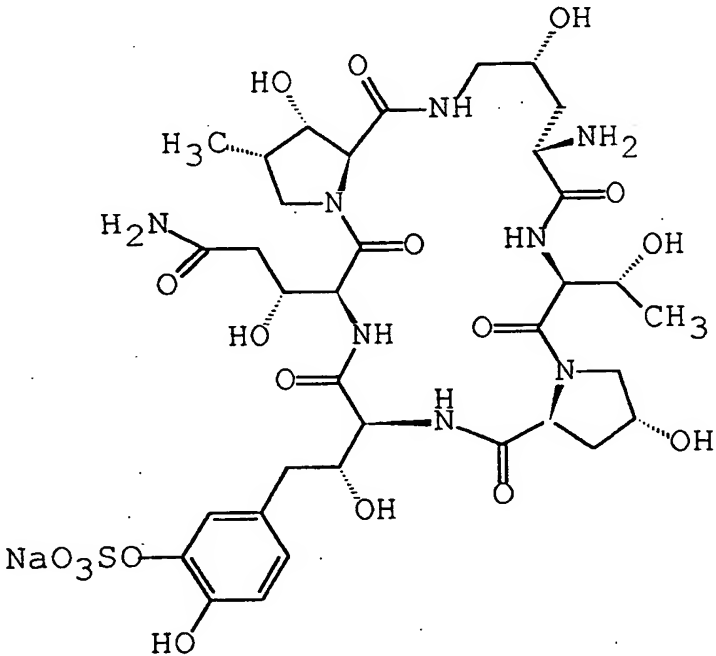
Example No.	Formula
	
2	

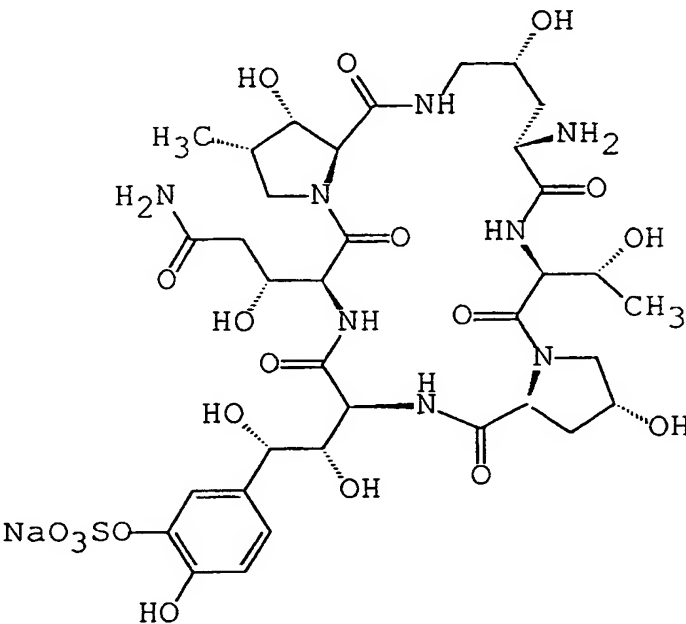
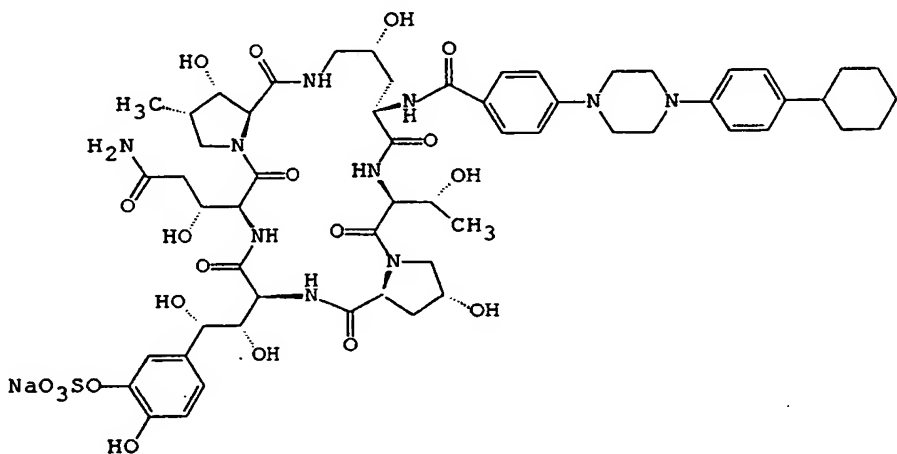
Example No.	Formula
	
3	

Example No.	Formula
4	
	

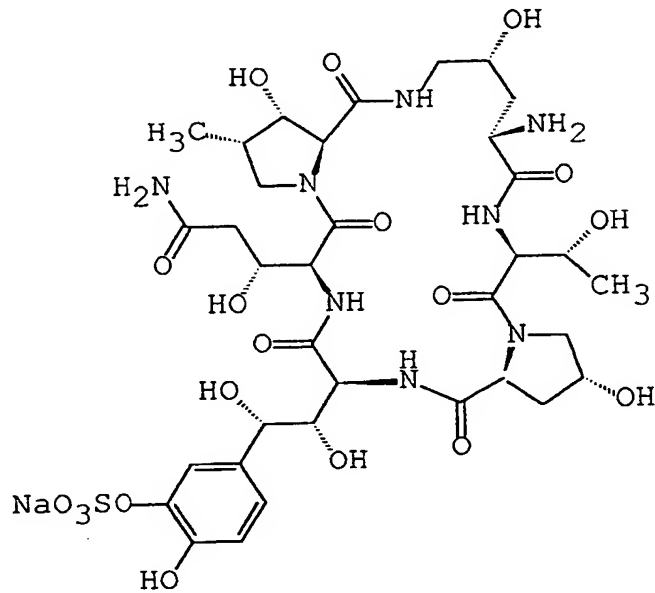
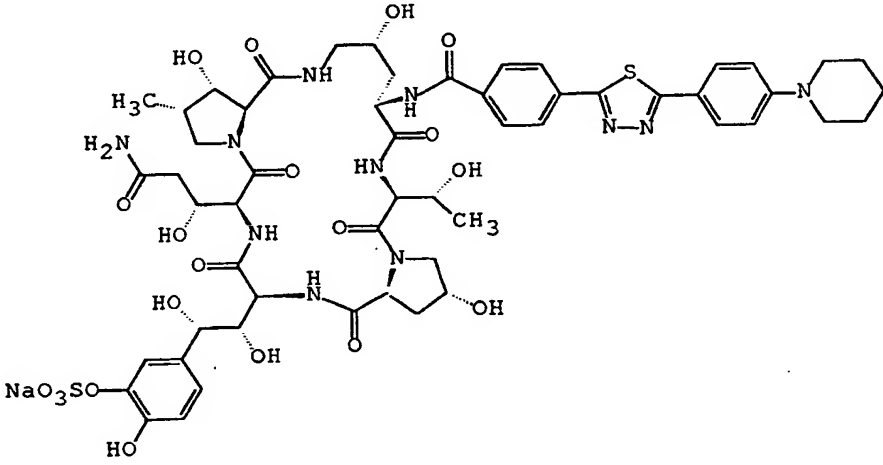
Example No.	Formula
5	
	

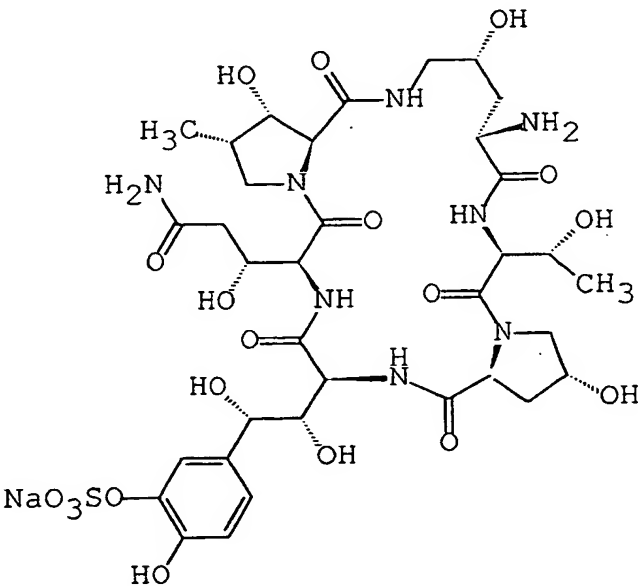
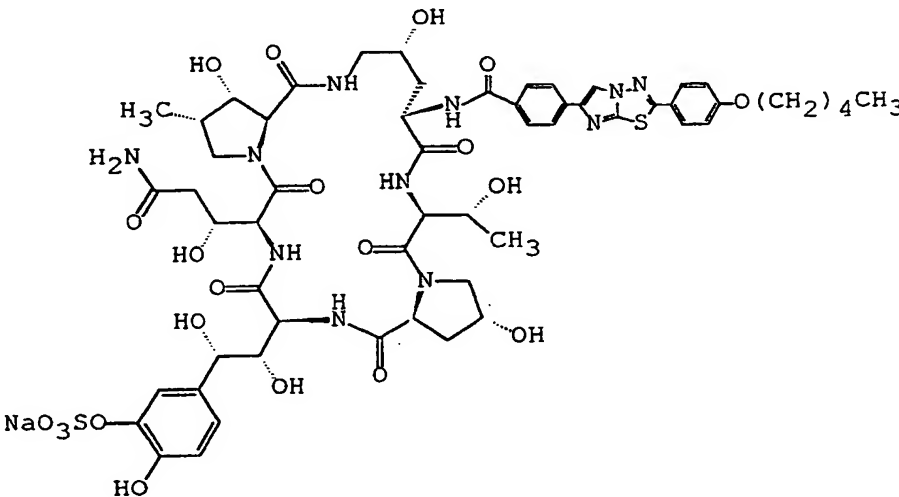
Example No.	Formula
6	
	

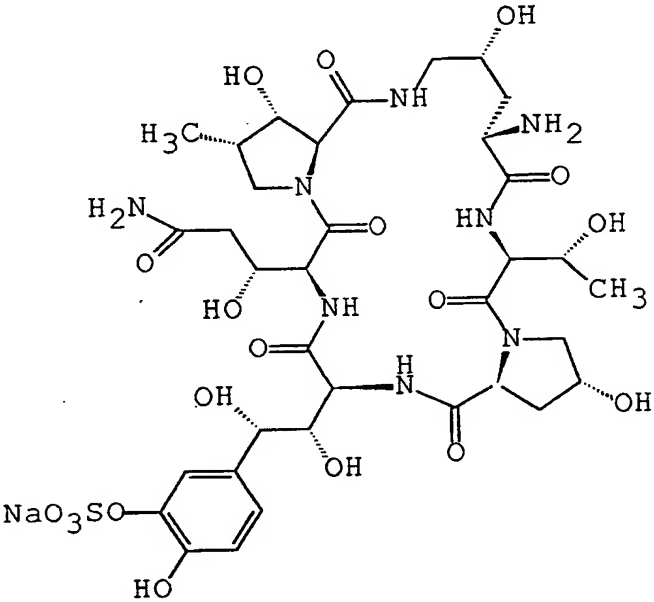
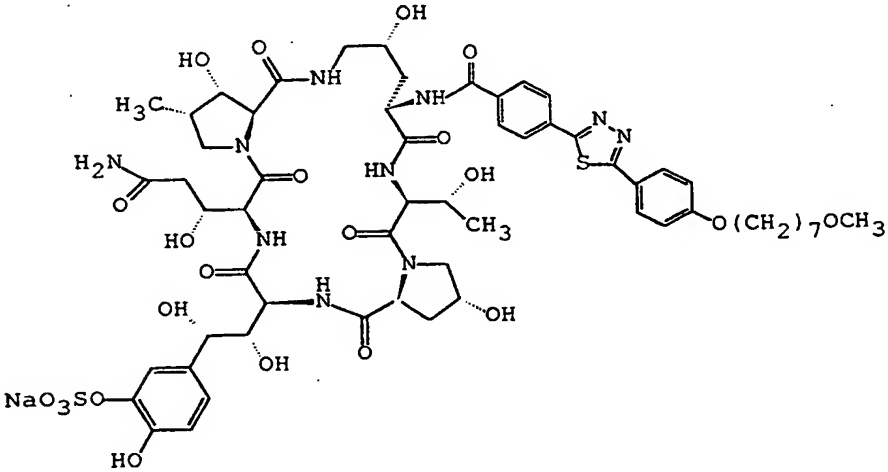
Example No.	Formula
7	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) attached to a benzene ring, a benzyl group (<math>\text{CH}_2\text{C}_6\text{H}_5</math>), and several hydroxyl (<math>\text{OH}</math>) and methyl (<math>\text{CH}_3</math>) groups. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>This chemical structure is similar to the one above, but it features a different substitution pattern. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) attached to a benzene ring, a benzyl group (<math>\text{CH}_2\text{C}_6\text{H}_5</math>), and several hydroxyl (<math>\text{OH}</math>) and methyl (<math>\text{CH}_3</math>) groups. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>

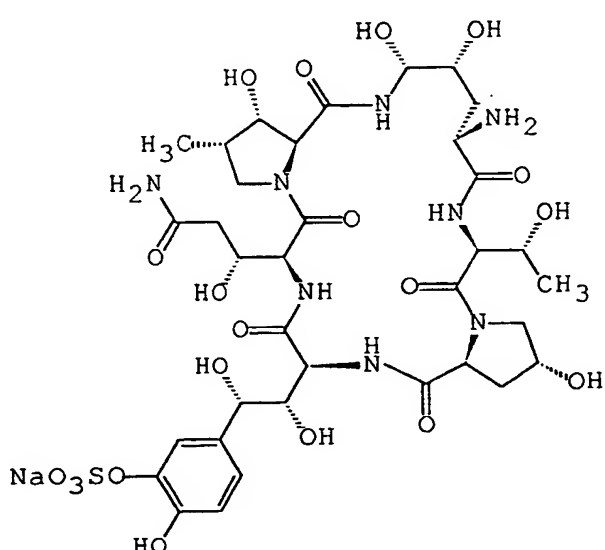
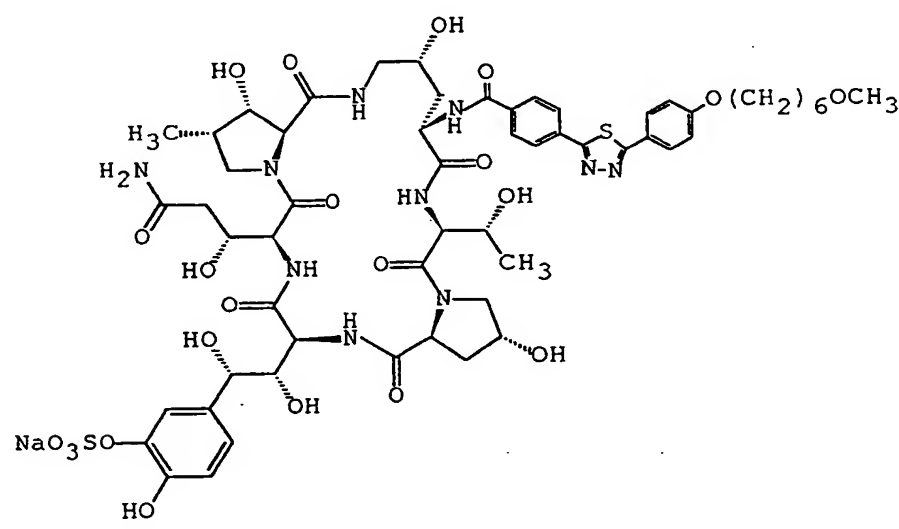
Example No.	Formula
8	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (NaO<sub>3</sub>SO-) attached to a benzene ring, which is further substituted with a hydroxyl group (HO-). The molecule also contains several hydroxyl groups (OH) and a methyl group (H<sub>3</sub>C). The structure is highly branched and contains multiple nitrogen atoms.</p>
	 <p>The chemical structure is a complex molecule, similar to the one above, but with a different side chain. It features a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (NaO<sub>3</sub>SO-) attached to a benzene ring, which is further substituted with a hydroxyl group (HO-). The molecule also contains several hydroxyl groups (OH) and a methyl group (H<sub>3</sub>C). The side chain is a long, branched structure with multiple amide and ester linkages, and a terminal group that appears to be a cyclohexyl ring.</p>

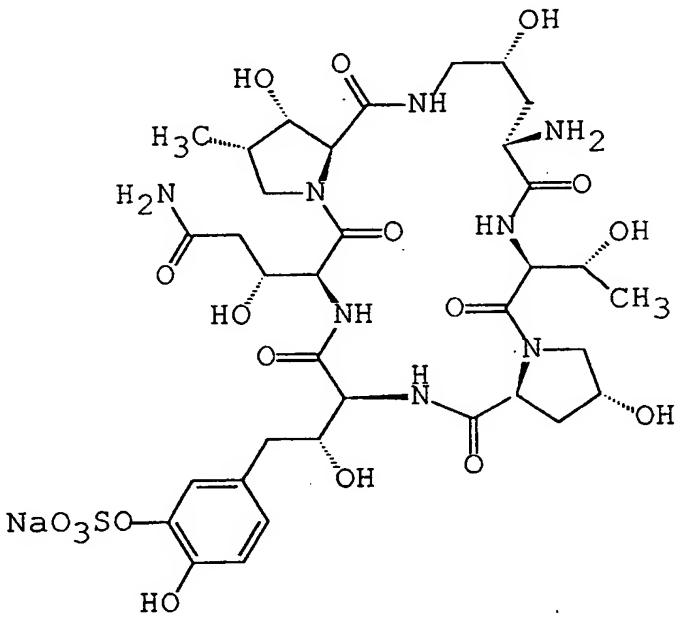
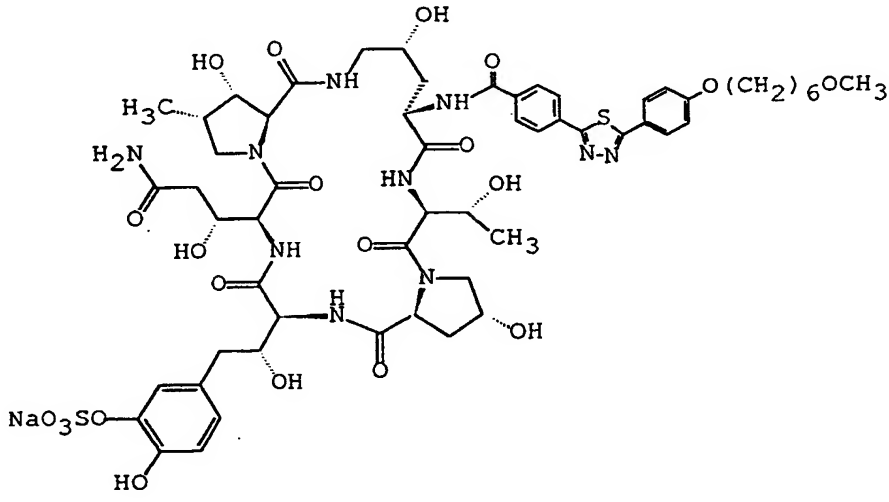


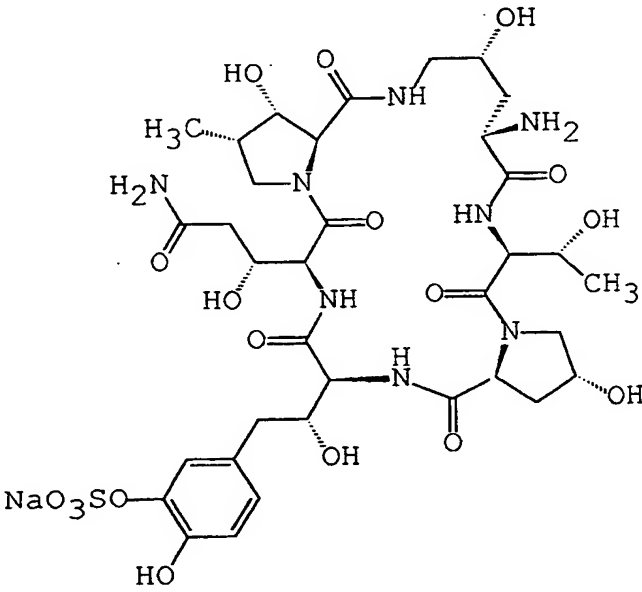
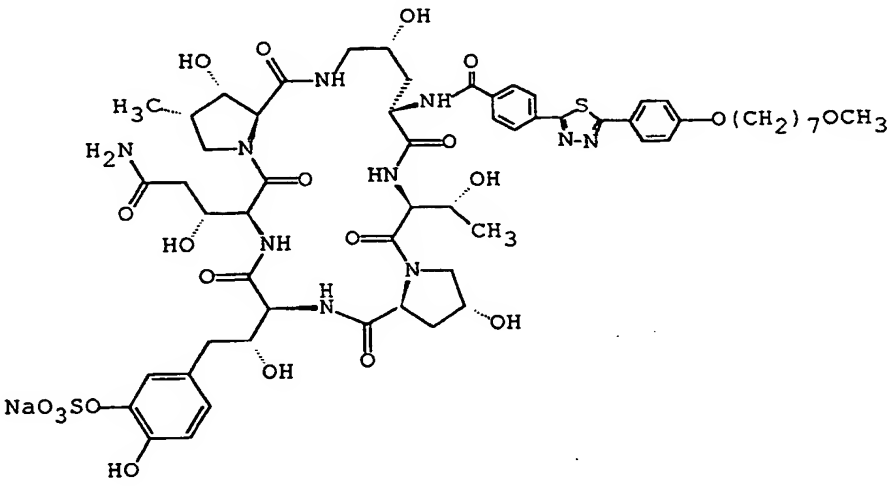
Example No.	Formula
9	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds. It also features a thiazole ring and a piperidine ring.</p>

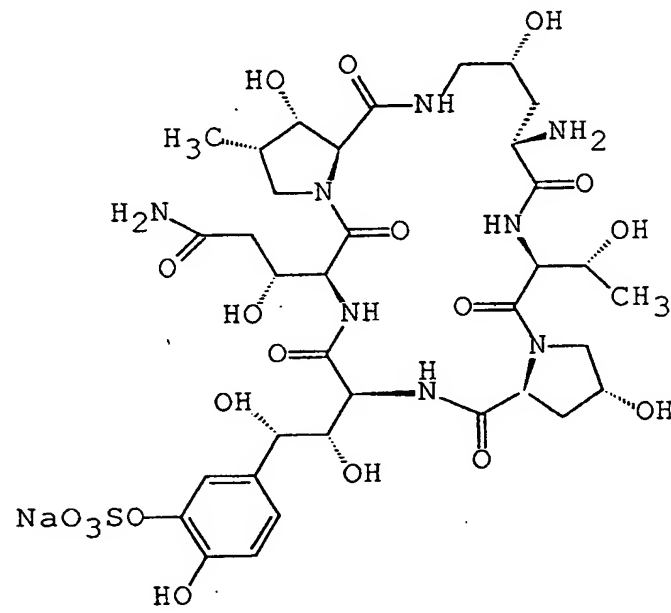
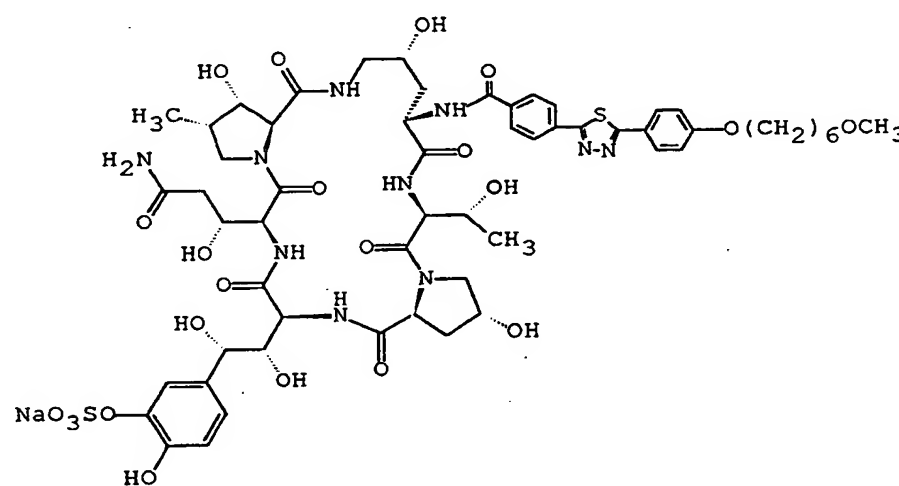
Example No.	Formula
10	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>The chemical structure is a complex molecule, similar to the one above, but with a different side chain. It features a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The side chain includes a triazole ring system and a long alkyl chain (<math>\text{O}(\text{CH}_2)_4\text{CH}_3</math>). The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>

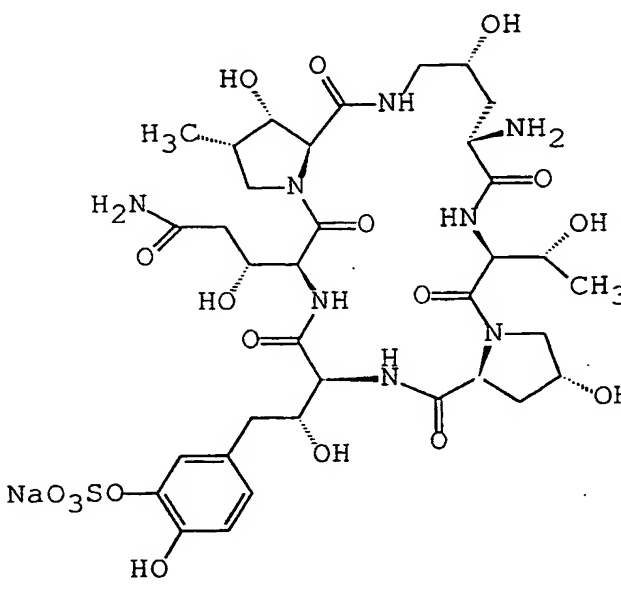
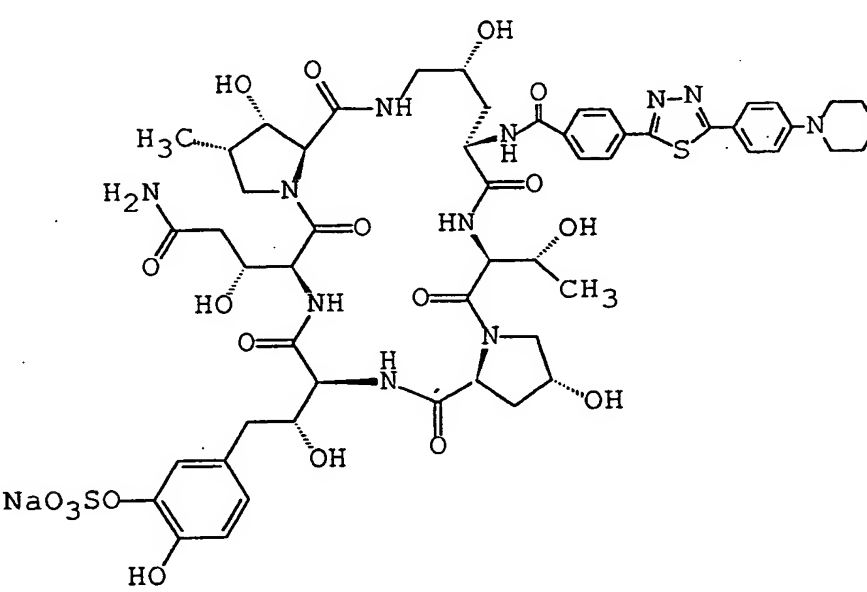
Example No.	Formula
11	
	

Example No.	Formula
12	
	

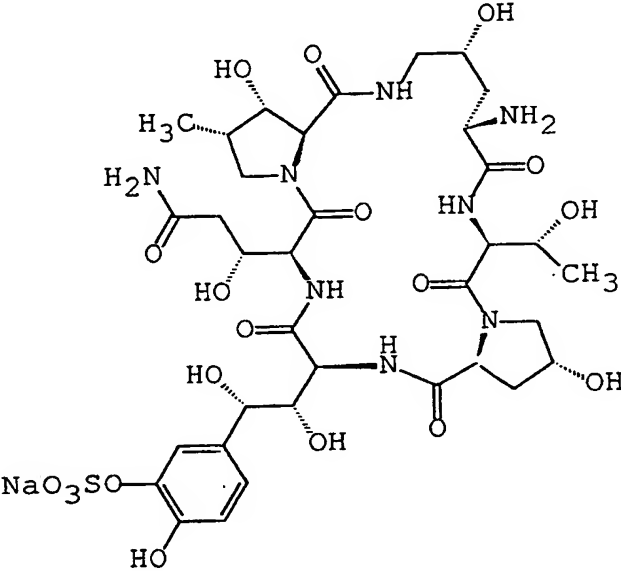
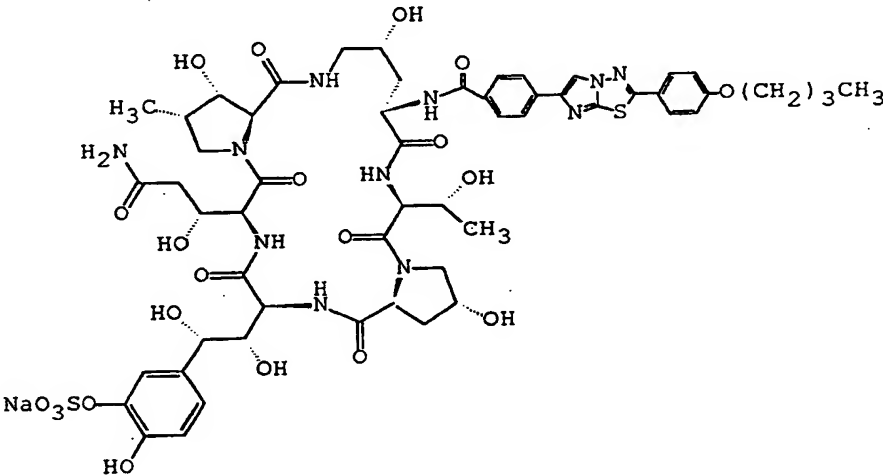
Example No.	Formula
13	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>The chemical structure is a complex molecule, similar to the one above, but with a different side chain. It features a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The side chain includes a benzene ring with a sulfonate group (<math>\text{SO}_3\text{Na}</math>) and a hydroxyl group (<math>\text{HO}</math>), and a long alkoxy chain (<math>\text{O}(\text{CH}_2)_6\text{OCH}_3</math>). The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>

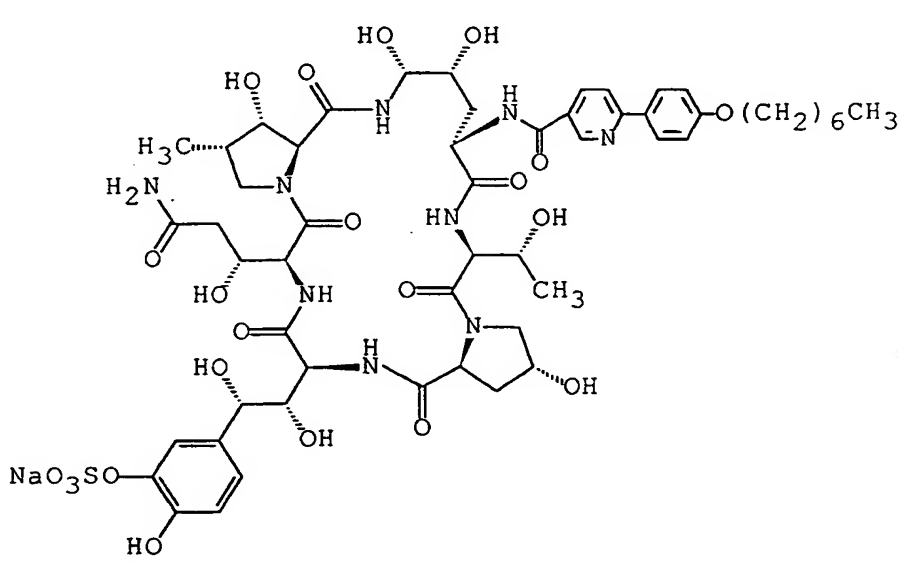
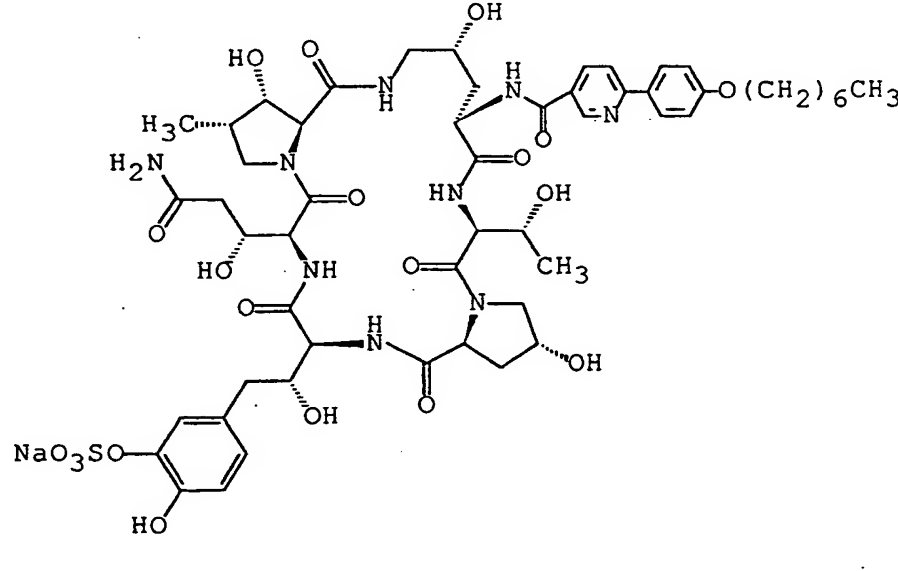
Example No.	Formula
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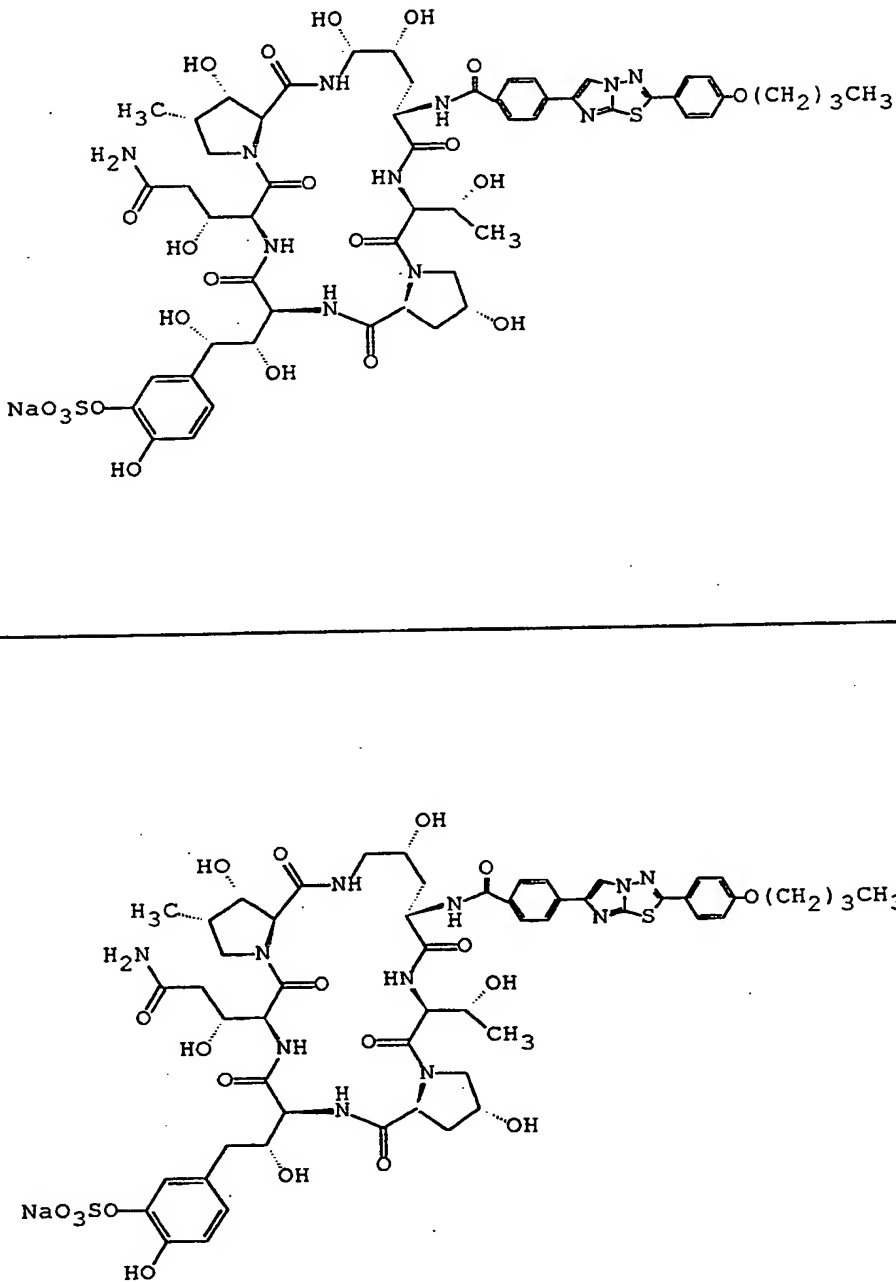
Example No.	Formula
15	 <p>The structure shows a complex molecule with multiple amide, hydroxyl, and sulfonate groups. It features a central chain with several amide linkages and hydroxyl groups. A sulfonate group (NaO<sub>3</sub>SO-) is attached to a phenyl ring, which is also substituted with a hydroxyl group. The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>The structure shows a complex molecule with multiple amide, hydroxyl, and sulfonate groups. It features a central chain with several amide linkages and hydroxyl groups. A sulfonate group (NaO<sub>3</sub>SO-) is attached to a phenyl ring, which is also substituted with a hydroxyl group. The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds. A long alkoxy chain (-(CH<sub>2</sub>)<sub>6</sub>OCH<sub>3</sub>) is attached to a phenyl ring via a sulfonamide linkage.</p>

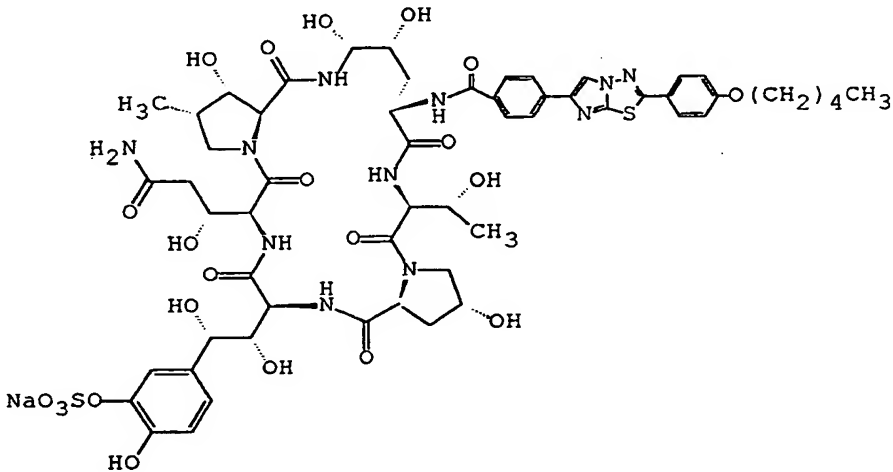
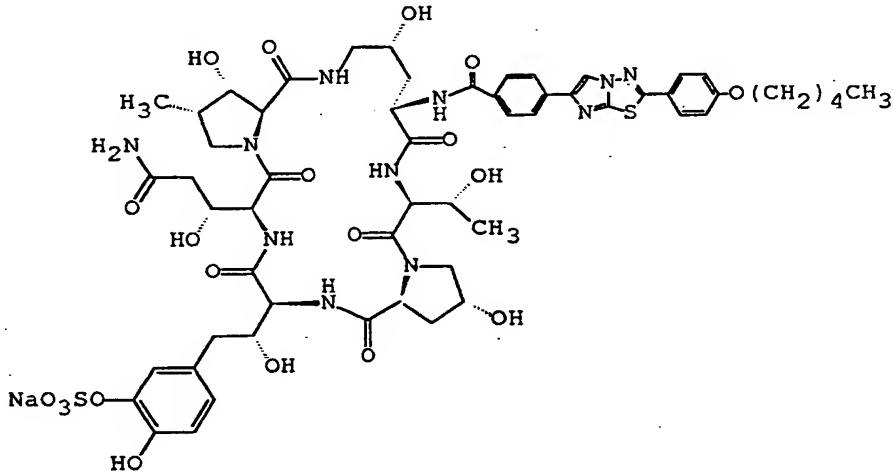
Example No.	Formula
16	 <p>The chemical structure shows a complex molecule with multiple fused and linked rings. It includes a piperidine ring, a pyrrolidine ring, and a benzene ring with a sulfonate group (NaO<sub>3</sub>SO-). The molecule is highly substituted with various functional groups, including amide, ester, and hydroxyl groups. Stereochemistry is indicated with wedges and dashes.</p>
	 <p>The chemical structure shows a complex molecule with multiple fused and linked rings. It includes a piperidine ring, a pyrrolidine ring, and a benzene ring with a sulfonate group (NaO<sub>3</sub>SO-). The molecule is highly substituted with various functional groups, including amide, ester, and hydroxyl groups. Stereochemistry is indicated with wedges and dashes.</p>

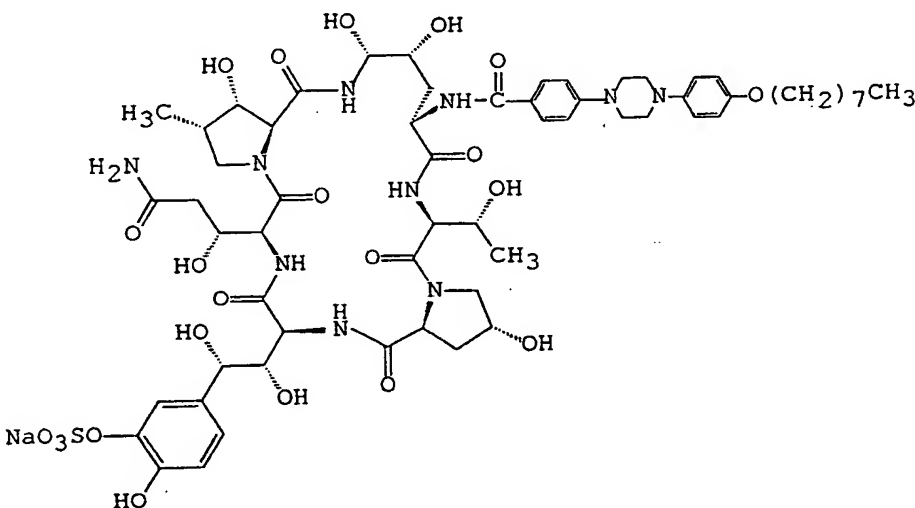
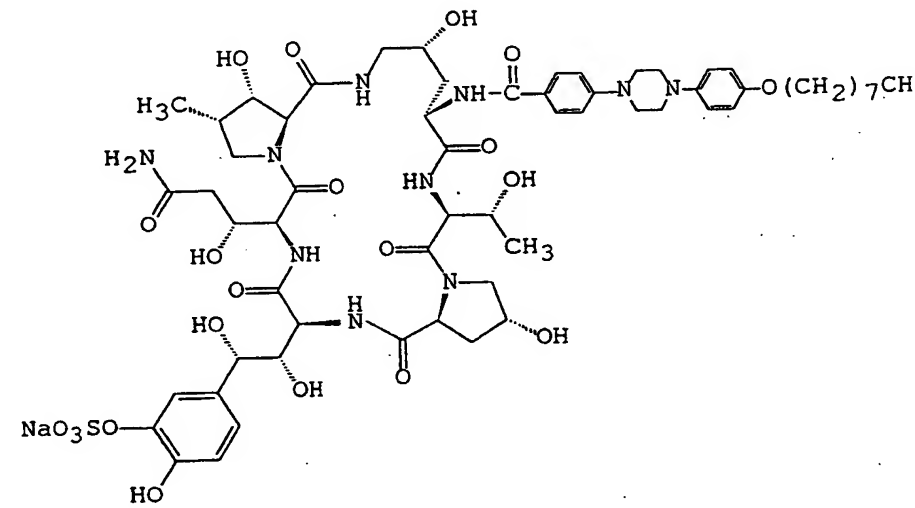


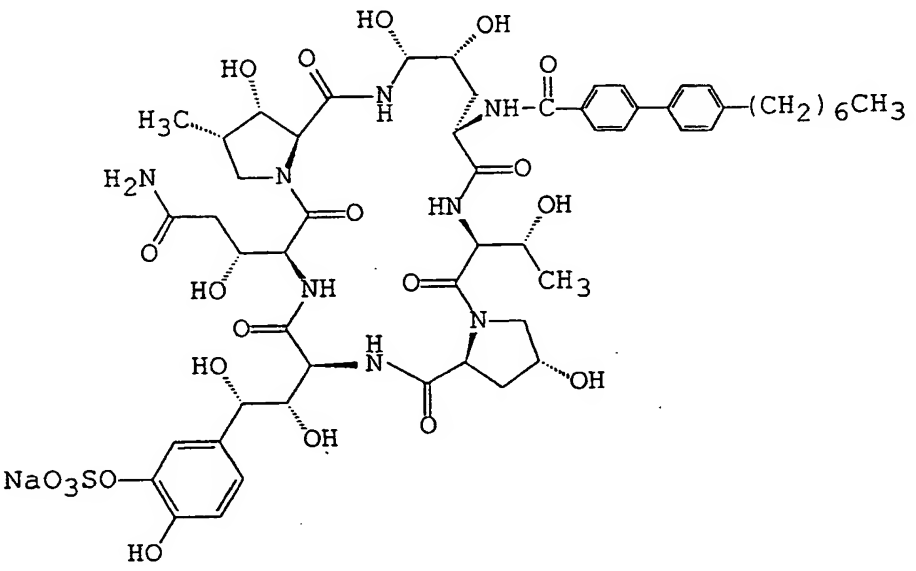
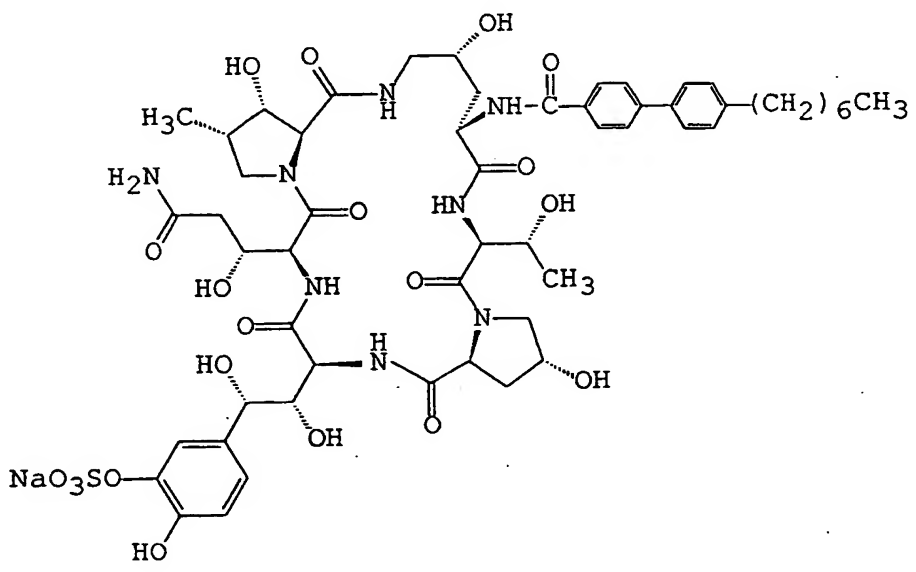
Example No.	Formula
17	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>The chemical structure is a complex molecule, similar to the one above, but with a different side chain. It features a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The side chain includes a thiazole ring and a long alkyl chain (<math>\text{O}(\text{CH}_2)_3\text{CH}_3</math>). The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>

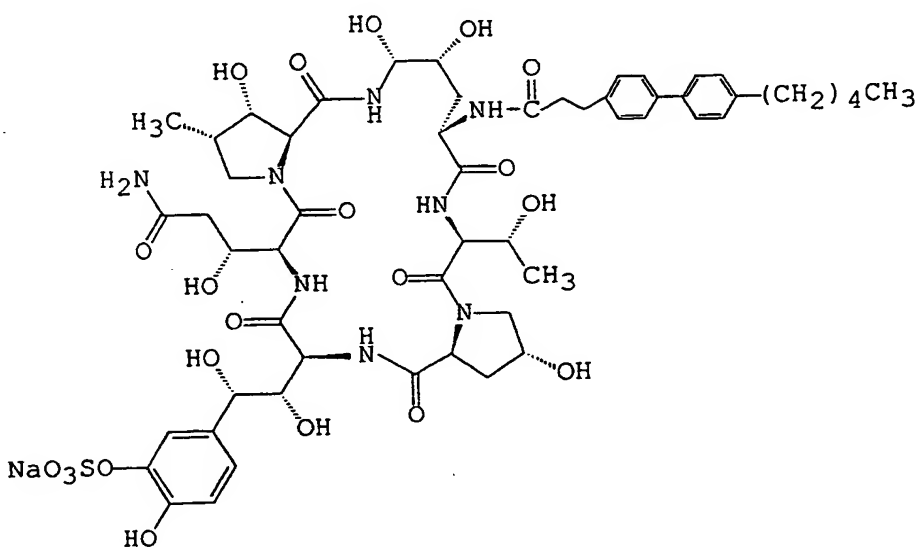
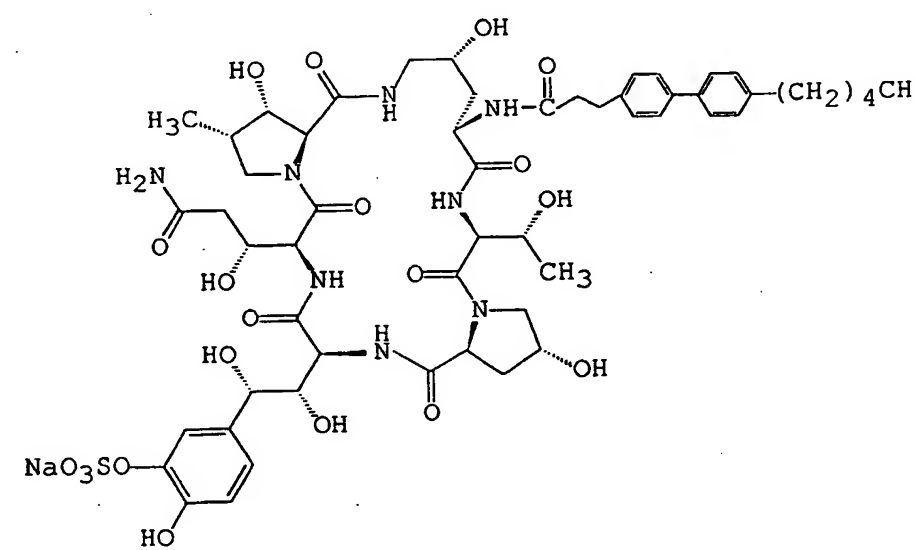
Example No.	Formula
18	
	

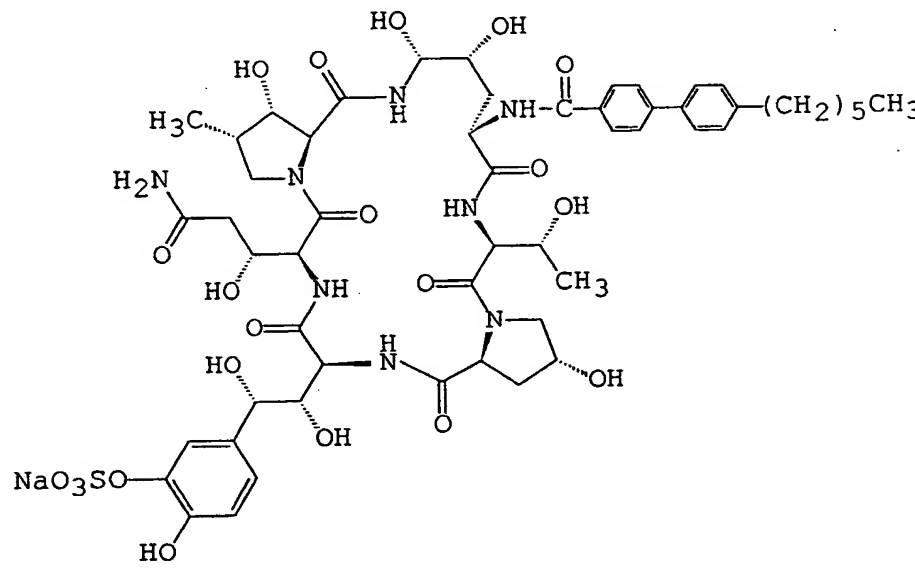
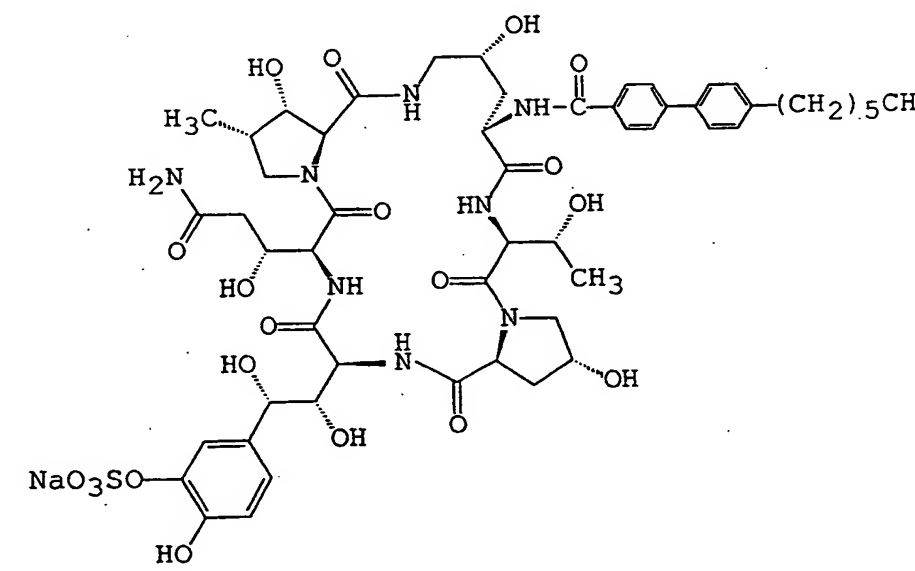
Example No.	Formula
19	 <p>The chemical structure represents a complex molecule, likely a cyclic peptide derivative. It features a central core with multiple amide bonds and hydroxyl groups. A prominent feature is a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) attached to a phenyl ring. The structure is shown in two identical representations, one above the other.</p>

Example No.	Formula
20	 <p>The chemical structure is a complex molecule with multiple stereocenters, amide bonds, and a sodium sulfonate group. It features a central core with various substituents, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The structure is shown in a perspective view with stereochemistry indicated by wedges and dashes.</p>
	 <p>The chemical structure is a complex molecule with multiple stereocenters, amide bonds, and a sodium sulfonate group. It features a central core with various substituents, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The structure is shown in a perspective view with stereochemistry indicated by wedges and dashes.</p>

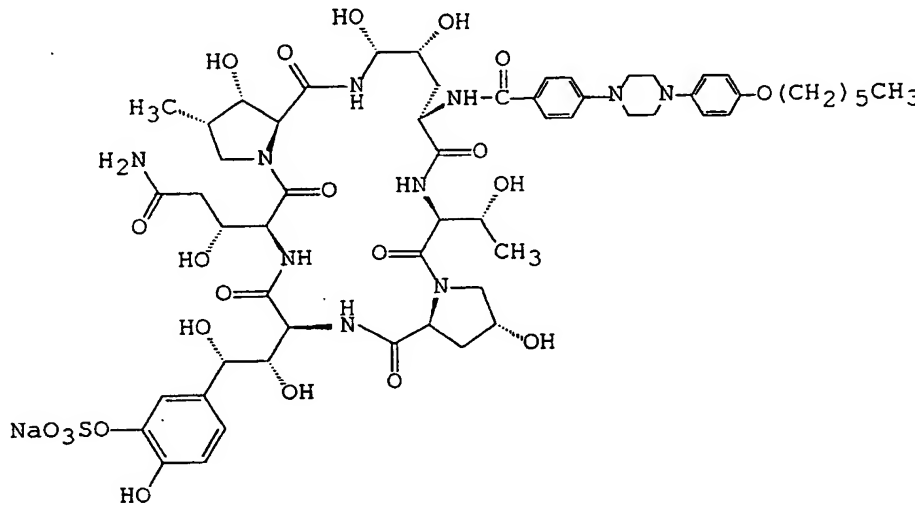
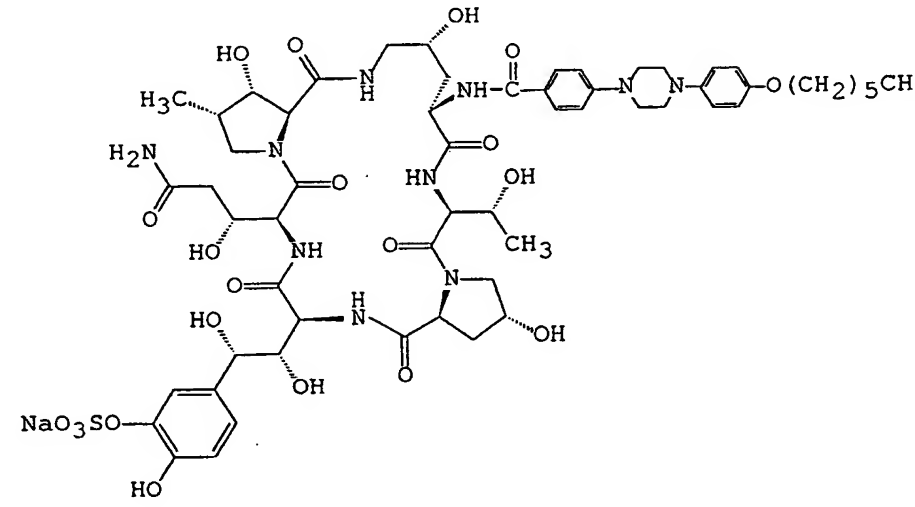
Example No.	Formula
	
21	

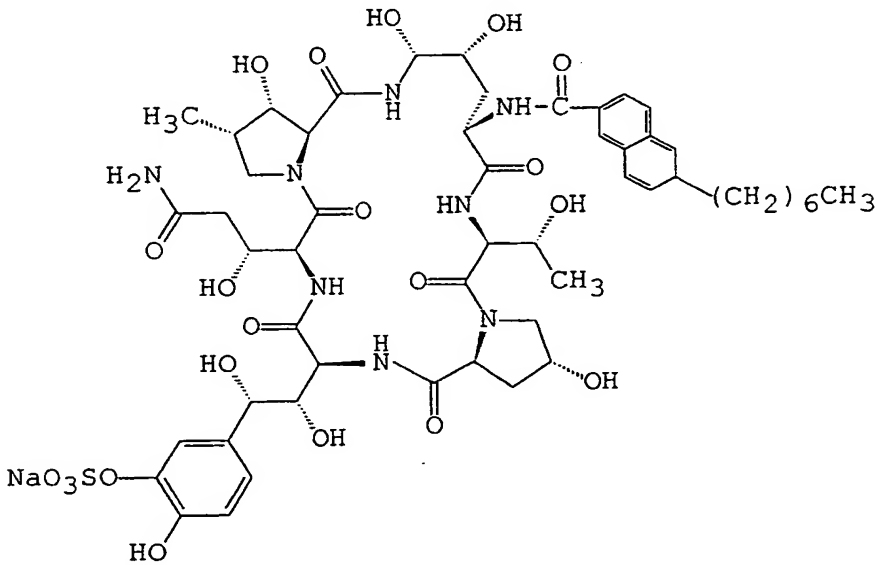
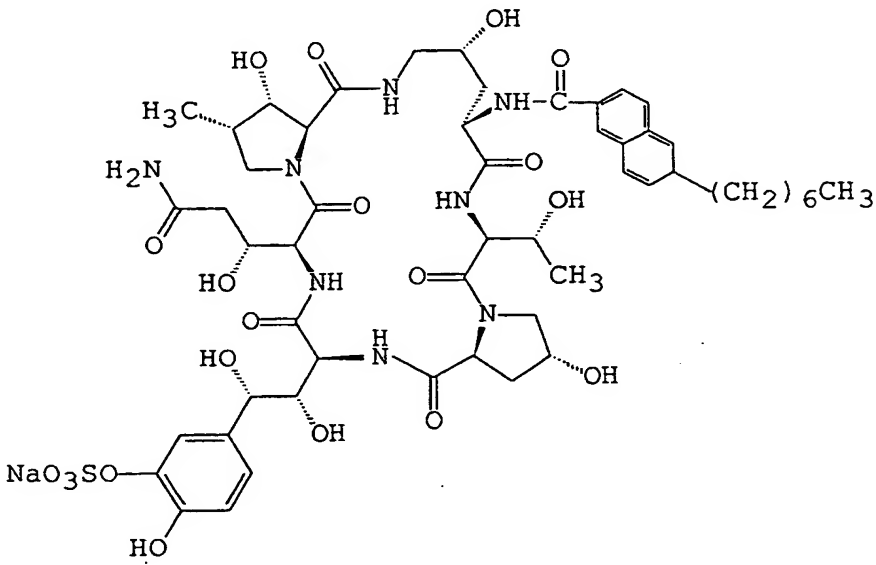
Example No.	Formula
	
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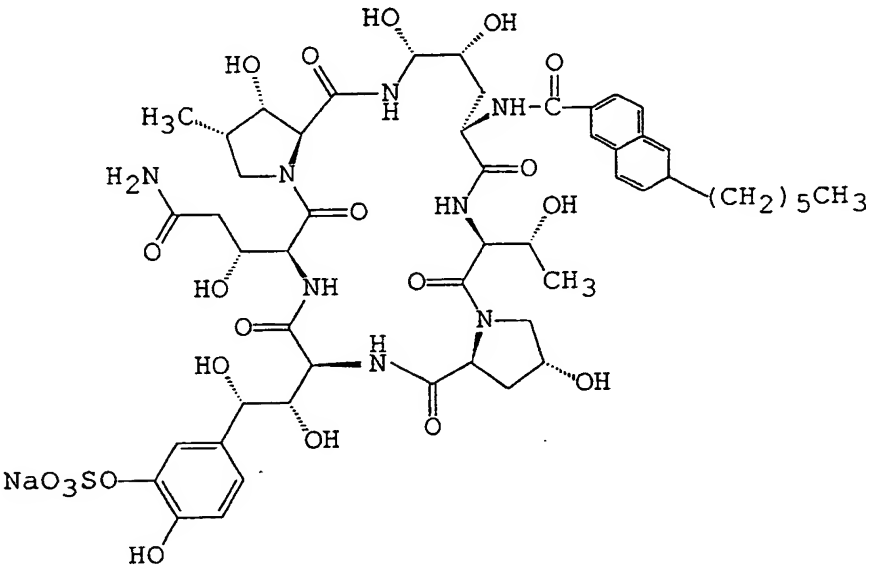
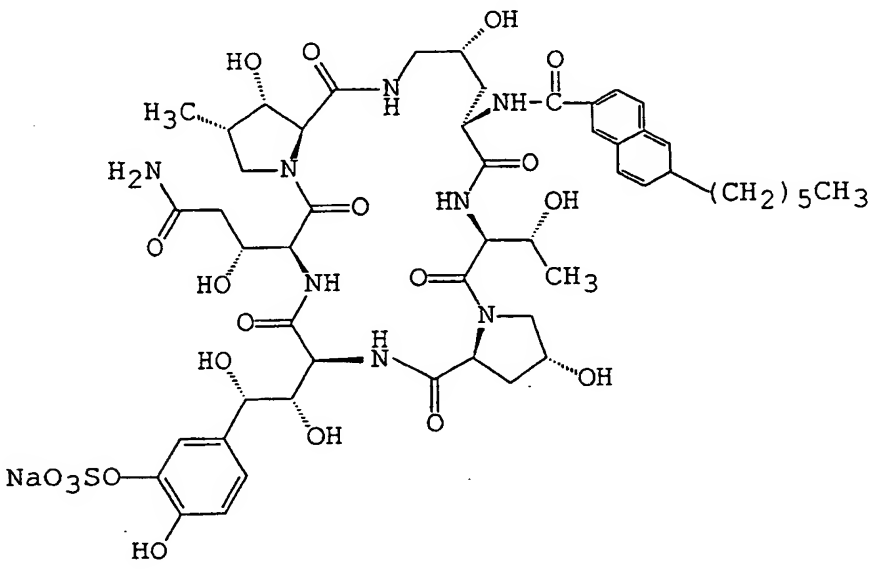
Example No.	Formula
	 <p>The chemical structure is a complex molecule featuring a central core of fused and linked rings. It includes a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a long alkyl chain (-(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>). The structure is highly detailed with various functional groups and stereochemical indicators.</p>
23	 <p>This chemical structure is identical to the one in the first row, showing a complex molecule with a p-toluenesulfonate group and a long alkyl chain.</p>

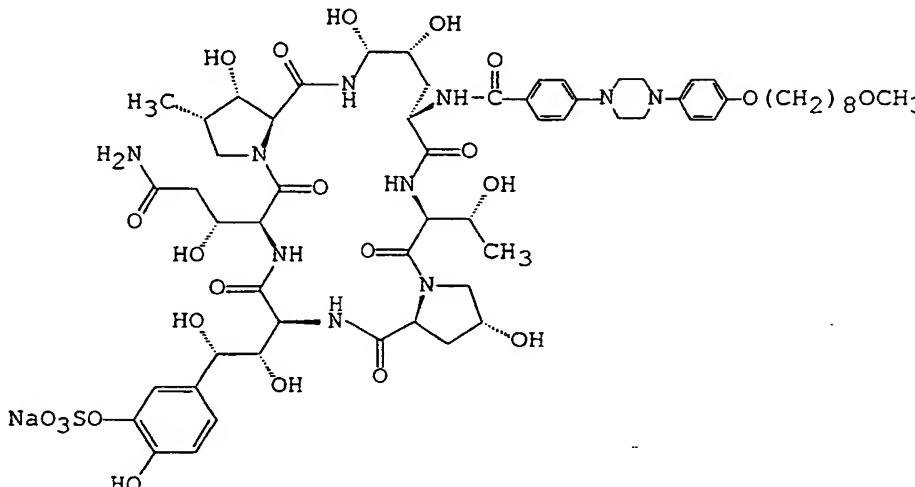
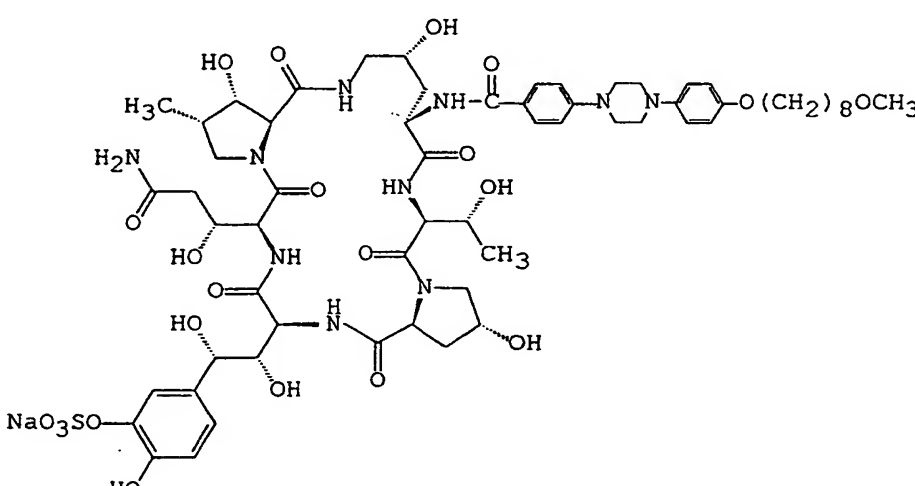
Example No.	Formula
	
24	

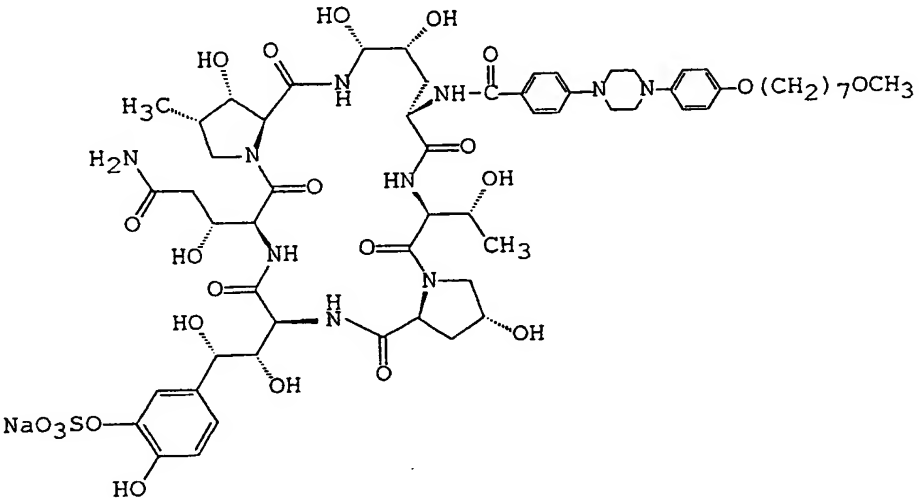
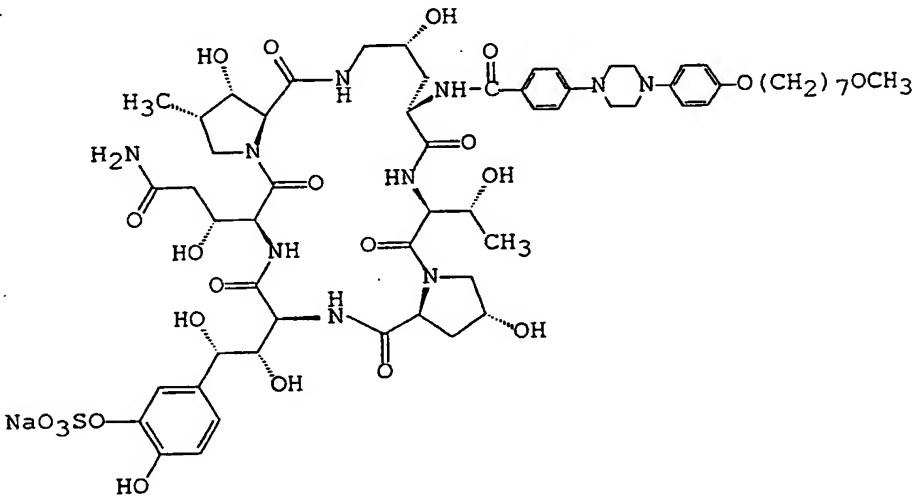


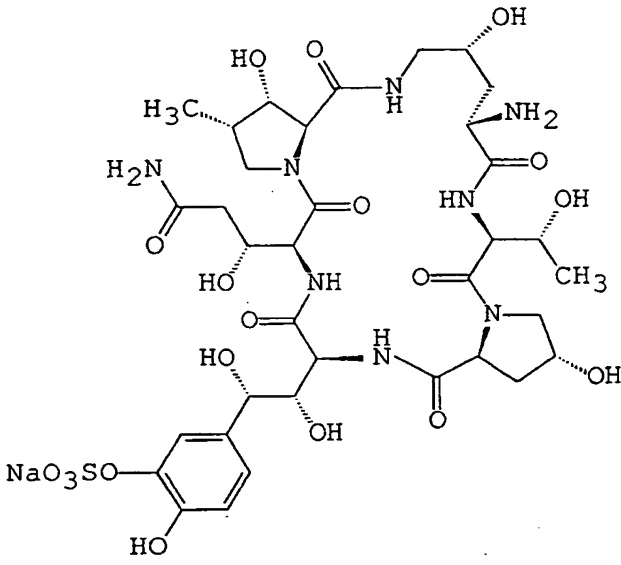
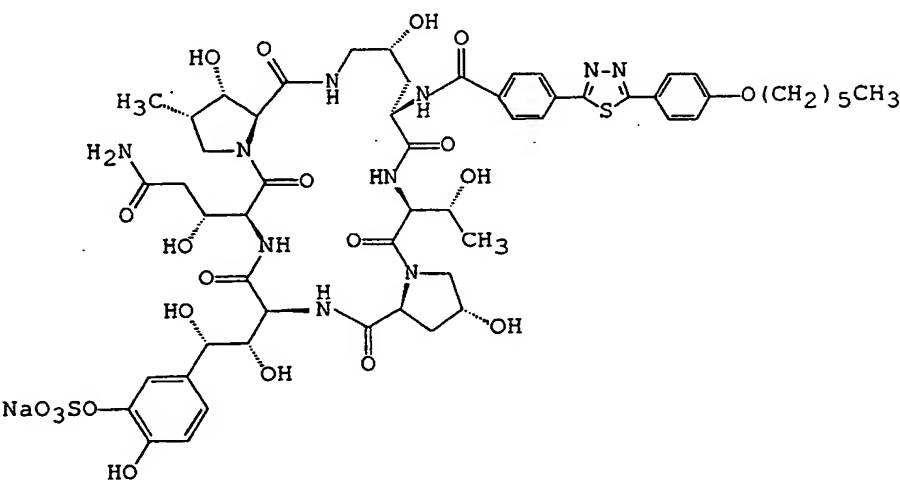
Example No.	Formula
25	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The structure also contains a piperazine ring and a long alkyl chain (<math>\text{O}(\text{CH}_2)_5\text{CH}_3</math>). Stereochemistry is indicated with wedges and dashes.</p>
	 <p>This chemical structure is identical to the one in the first row, showing a complex molecule with multiple amide and ester linkages, a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>), a hydroxyl group (<math>\text{HO}</math>), a piperazine ring, and a long alkyl chain (<math>\text{O}(\text{CH}_2)_5\text{CH}_3</math>). Stereochemistry is indicated with wedges and dashes.</p>

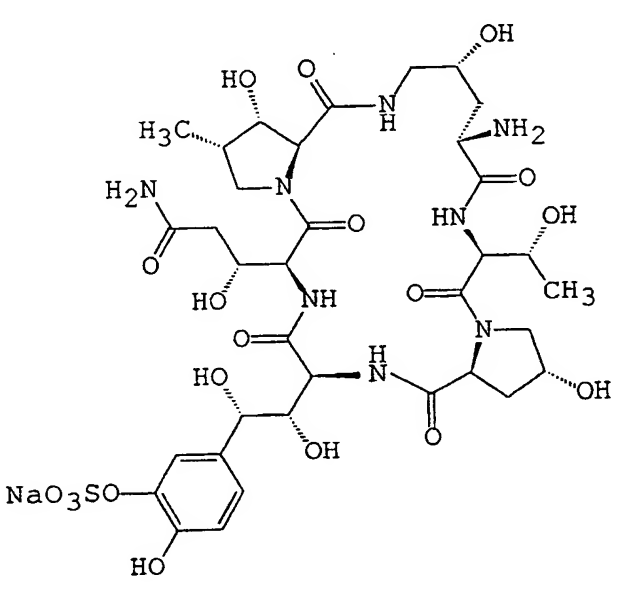
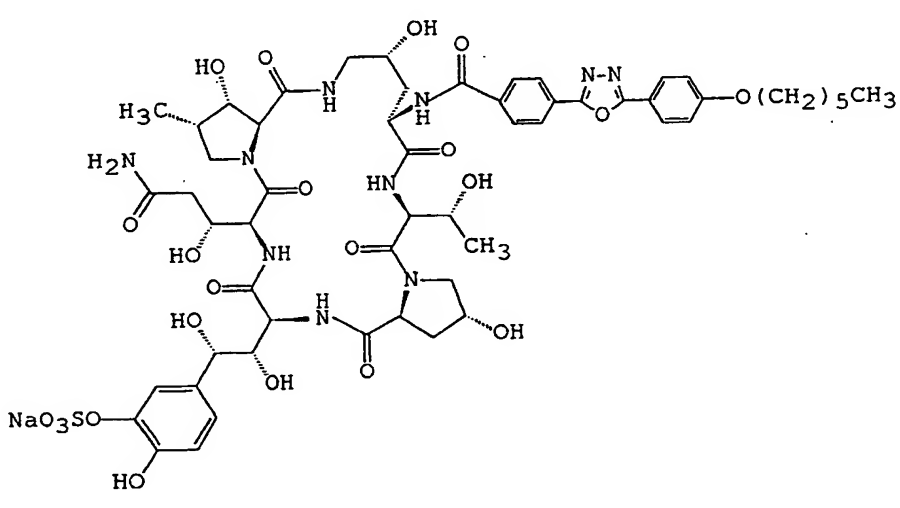
Example No.	Formula
	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}-</math>) attached to a phenyl ring, a long alkyl chain <math>(\text{CH}_2)_6\text{CH}_3</math>, and several hydroxyl (<math>\text{OH}</math>) and methyl (<math>\text{CH}_3</math>) groups. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
26	 <p>This chemical structure is identical to the one in the first row, showing a complex molecule with multiple amide, ester, and hydroxyl groups, including a sodium sulfonate group and a long alkyl chain.</p>

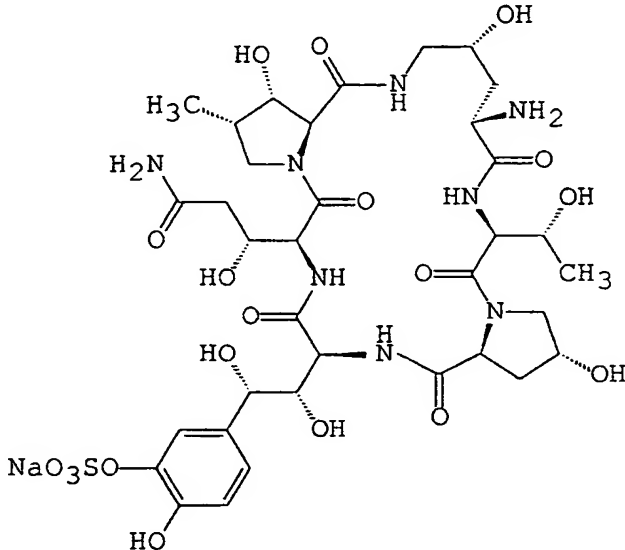
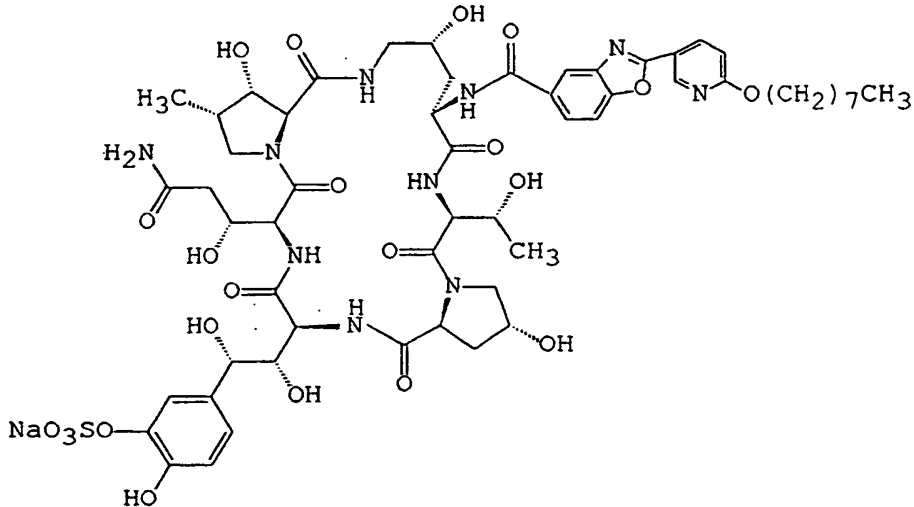
Example No.	Formula
	 <p>The chemical structure is a complex molecule with multiple stereocenters, amide bonds, and a sodium sulfonate group. It features a central core with various substituents, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The structure is drawn with stereochemistry indicated by wedges and dashes.</p>
27	 <p>The chemical structure is identical to the one in the first row, showing a complex molecule with multiple stereocenters, amide bonds, and a sodium sulfonate group. It features a central core with various substituents, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The structure is drawn with stereochemistry indicated by wedges and dashes.</p>

Example No.	Formula
	
28	

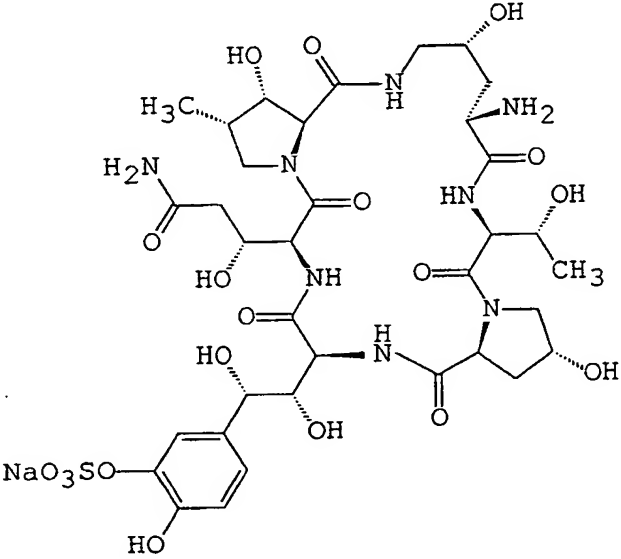
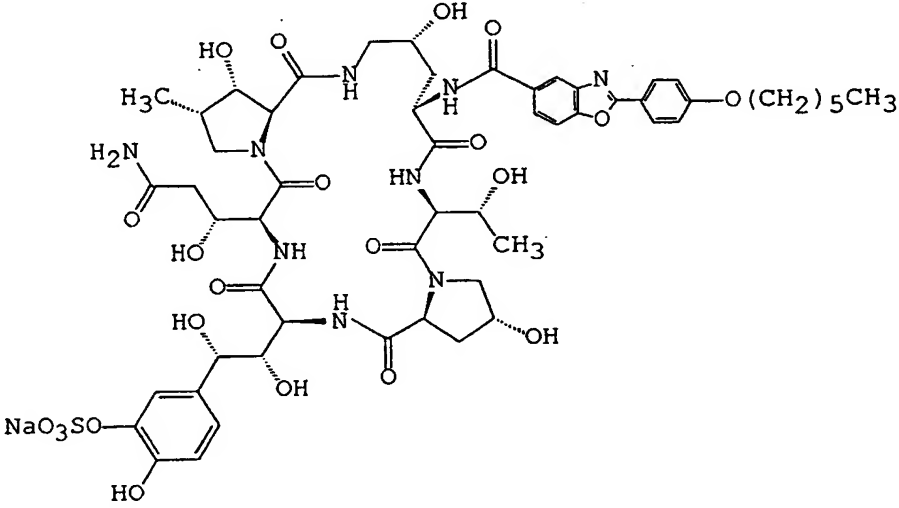
Example No.	Formula
	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a long alkoxy chain (O(CH<sub>2</sub>)<sub>7</sub>OCH<sub>3</sub>). The molecule is highly branched and contains several hydroxyl groups.</p>
29	 <p>The chemical structure is identical to the one in the first row, showing a complex molecule with multiple amide and ester linkages, a p-toluenesulfonate group (NaO<sub>3</sub>SO-), and a long alkoxy chain (O(CH<sub>2</sub>)<sub>7</sub>OCH<sub>3</sub>).</p>

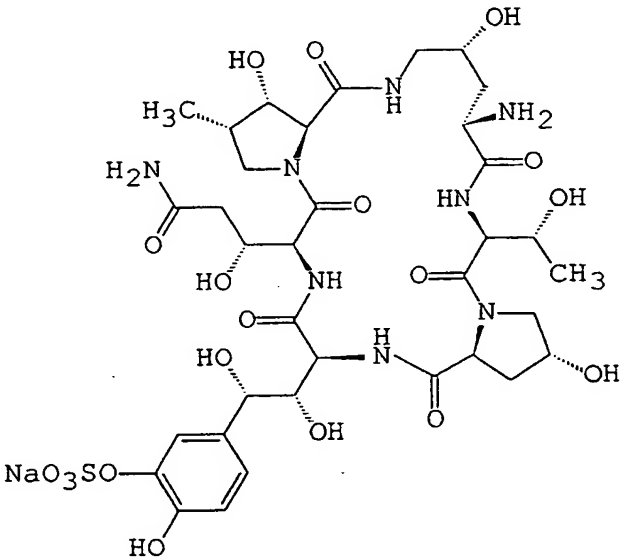
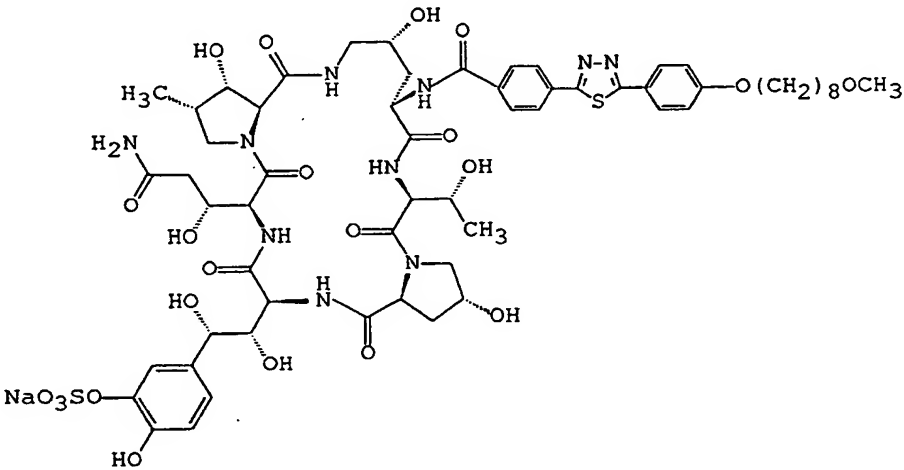
Example No.	Formula
30	 <p>The chemical structure is a complex molecule featuring a central core with multiple rings and functional groups. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>), a hydroxyl group (<math>\text{HO}</math>), and a methyl group (<math>\text{H}_3\text{C}</math>). The structure is highly branched and contains several amide and ester linkages.</p>
	 <p>The chemical structure is a complex molecule featuring a central core with multiple rings and functional groups. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>), a hydroxyl group (<math>\text{HO}</math>), and a methyl group (<math>\text{H}_3\text{C}</math>). The structure is highly branched and contains several amide and ester linkages. It also features a long alkyl chain (<math>\text{O}(\text{CH}_2)_5\text{CH}_3</math>) and a thiazole ring system.</p>

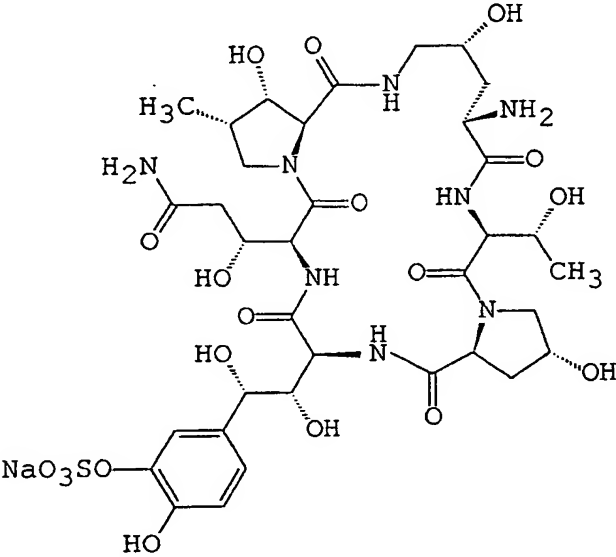
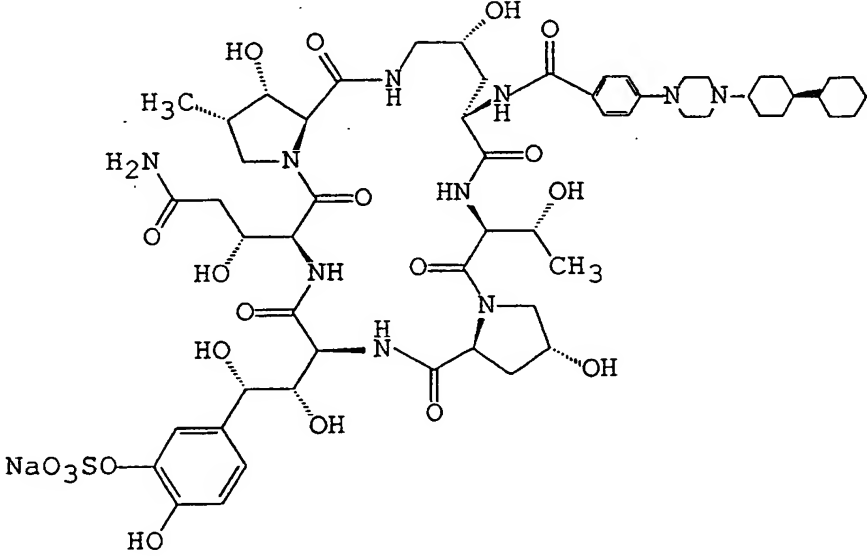
Example No.	Formula
	
31	

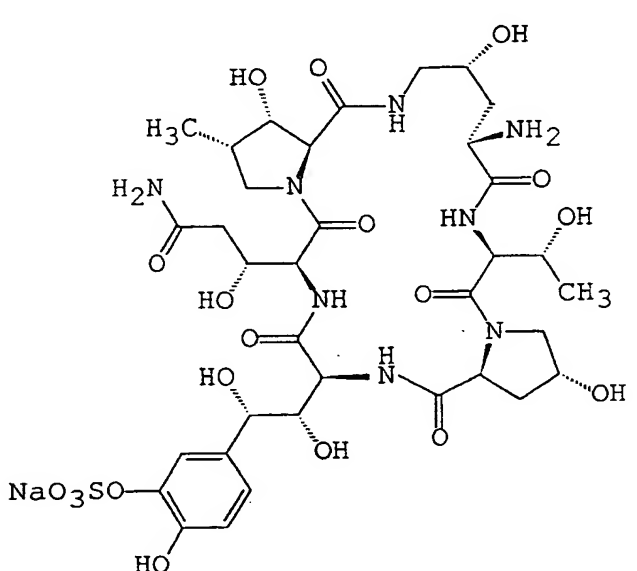
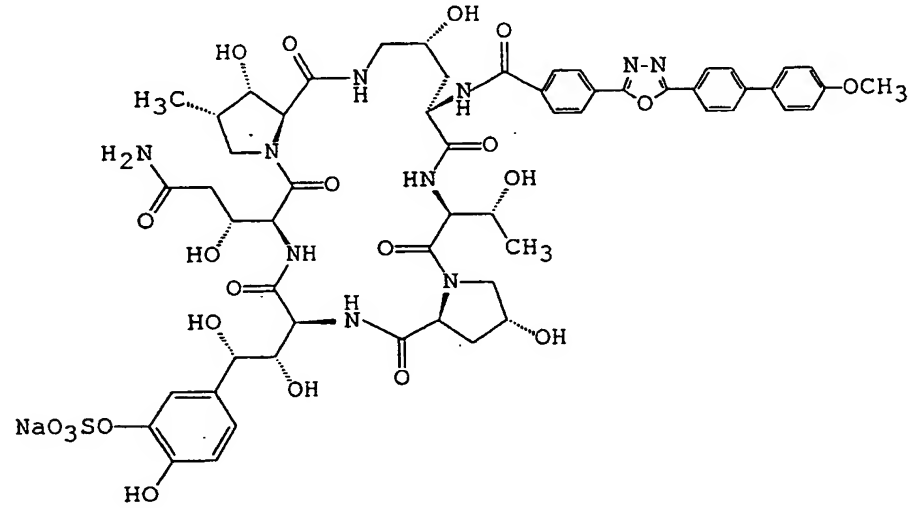
Example No.	Formula
	
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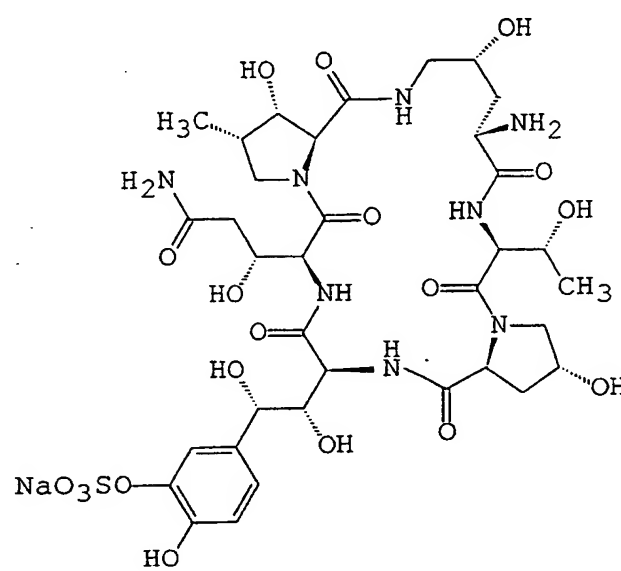
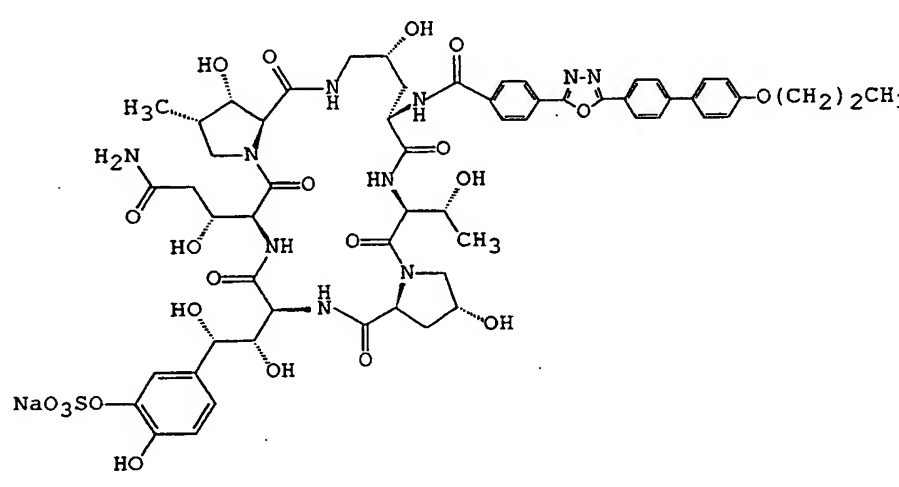


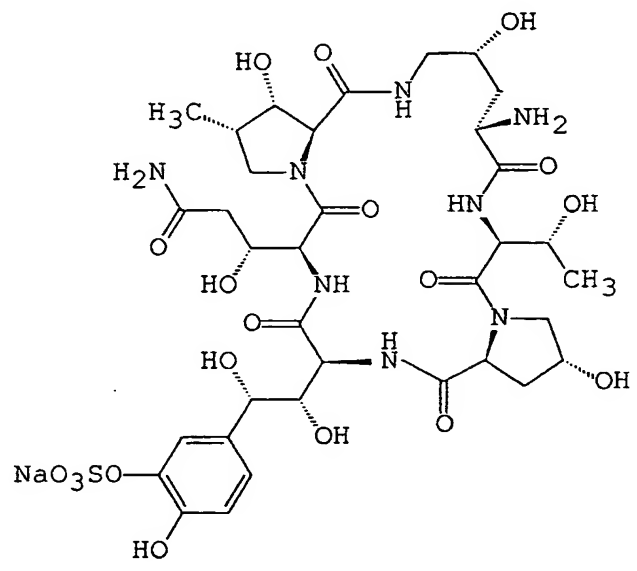
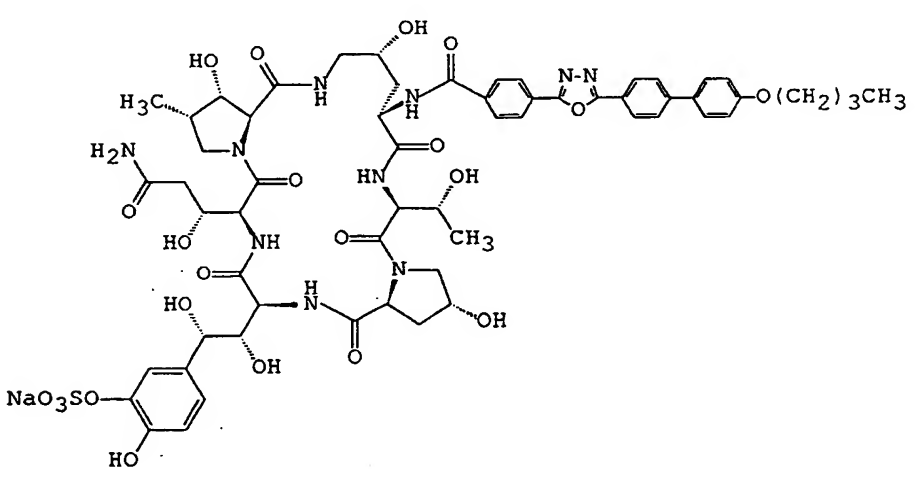
Example No.	Formula
	 <p>The structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. Other features include a methyl group (<math>\text{H}_3\text{C}</math>), a hydroxyl group (<math>\text{OH}</math>), and a hydroxyl group (<math>\text{OH}</math>) on a cyclopentane ring. The molecule is highly branched and contains several chiral centers.</p>
33	 <p>The structure is a complex molecule, similar to the one above, but with a different side chain. It features a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The side chain includes a methyl group (<math>\text{H}_3\text{C}</math>), a hydroxyl group (<math>\text{OH}</math>), and a hydroxyl group (<math>\text{OH}</math>) on a cyclopentane ring. The molecule is highly branched and contains several chiral centers.</p>

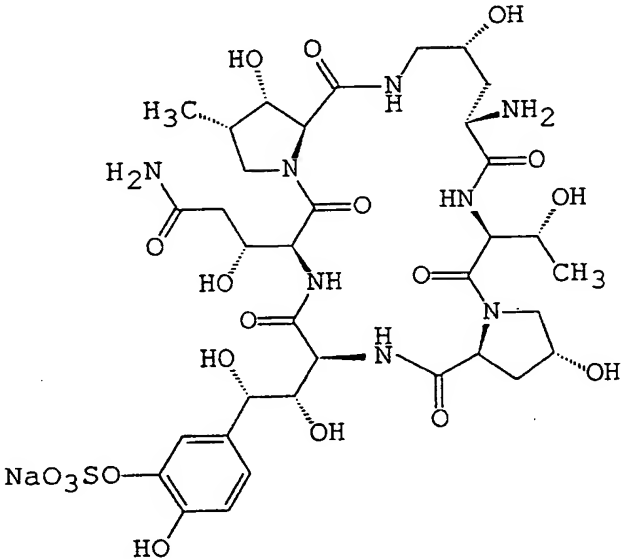
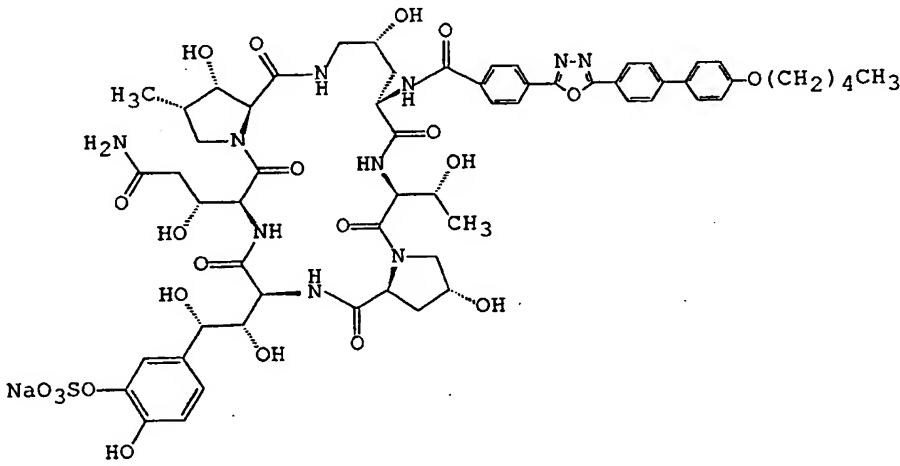
Example No.	Formula
	 <p>Chemical structure of a complex molecule, likely a derivative of a natural product. The structure features a central amide linkage connecting two main fragments. The left fragment includes a hydroxyl group, a methyl group, and a sodium sulfonate group (NaO<sub>3</sub>SO-). The right fragment includes a hydroxyl group, a methyl group, and a sodium sulfonate group (NaO<sub>3</sub>SO-). The molecule is highly branched and contains several amide and ester functional groups.</p>
34	 <p>Chemical structure of a complex molecule, similar to the one above, but with a different side chain. The structure features a central amide linkage connecting two main fragments. The left fragment includes a hydroxyl group, a methyl group, and a sodium sulfonate group (NaO<sub>3</sub>SO-). The right fragment includes a hydroxyl group, a methyl group, and a sodium sulfonate group (NaO<sub>3</sub>SO-). The molecule is highly branched and contains several amide and ester functional groups.</p>

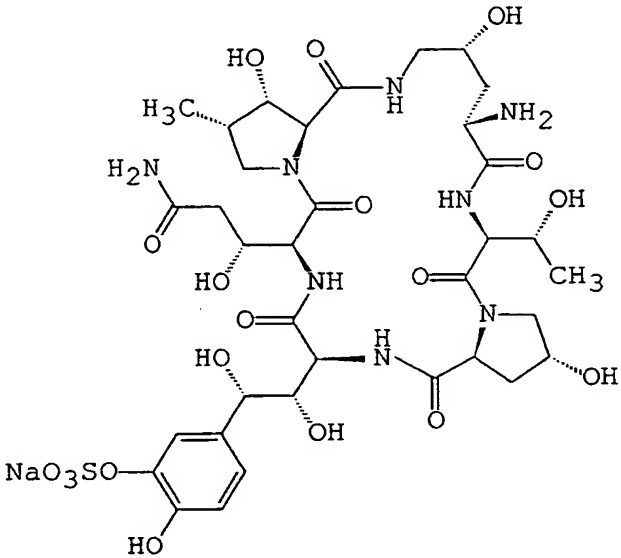
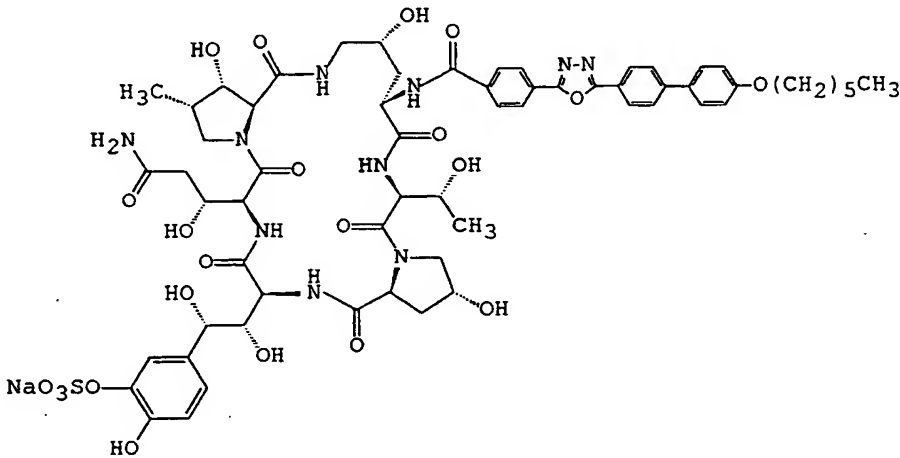
Example No.	Formula
35	 <p>The structure is a complex molecule featuring a central core with multiple amide and hydroxyl groups. It includes a methyl group (H<sub>3</sub>C) and a 4-hydroxy-3-sulfonatophenyl group (NaO<sub>3</sub>SO-C<sub>6</sub>H<sub>4</sub>-OH). The molecule is highly branched with various functional groups.</p>
	 <p>This structure is similar to the one above, but it features a different side chain. It includes a methyl group (H<sub>3</sub>C) and a 4-hydroxy-3-sulfonatophenyl group (NaO<sub>3</sub>SO-C<sub>6</sub>H<sub>4</sub>-OH). The molecule is highly branched with various functional groups.</p>

Example No.	Formula
	
36	

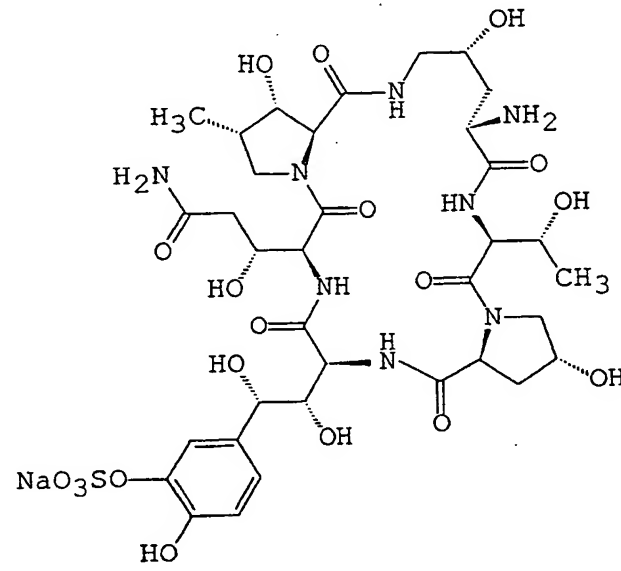
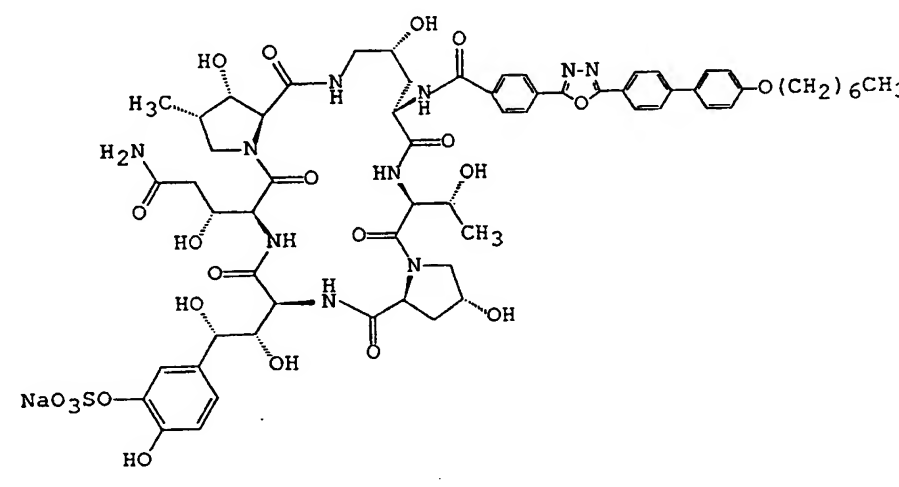
Example No.	Formula
	
37	

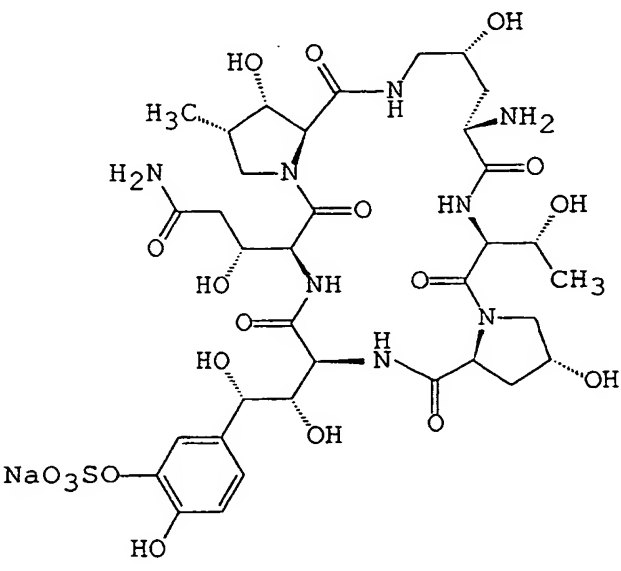
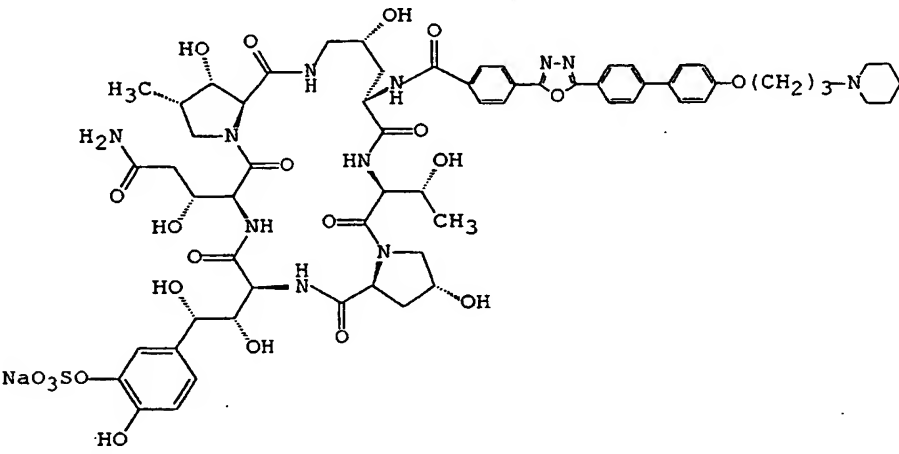
Example No.	Formula
	 <p>The structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. Other functional groups include a methyl group (<math>\text{H}_3\text{C}</math>), a hydroxyl group (<math>\text{OH}</math>), and a carboxamide group (<math>\text{H}_2\text{N}</math>).</p>
38	 <p>This structure is similar to the one above, but it features a different side chain. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The side chain is a long, flexible chain containing a hydroxyl group (<math>\text{OH}</math>), a carboxamide group (<math>\text{H}_2\text{N}</math>), and a methyl group (<math>\text{CH}_3</math>). The chain ends with a hydroxyl group (<math>\text{OH}</math>) and a methyl group (<math>\text{CH}_3</math>).</p>

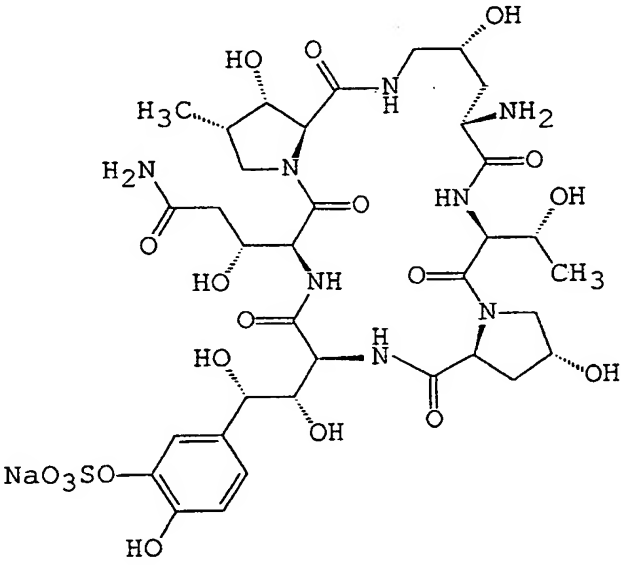
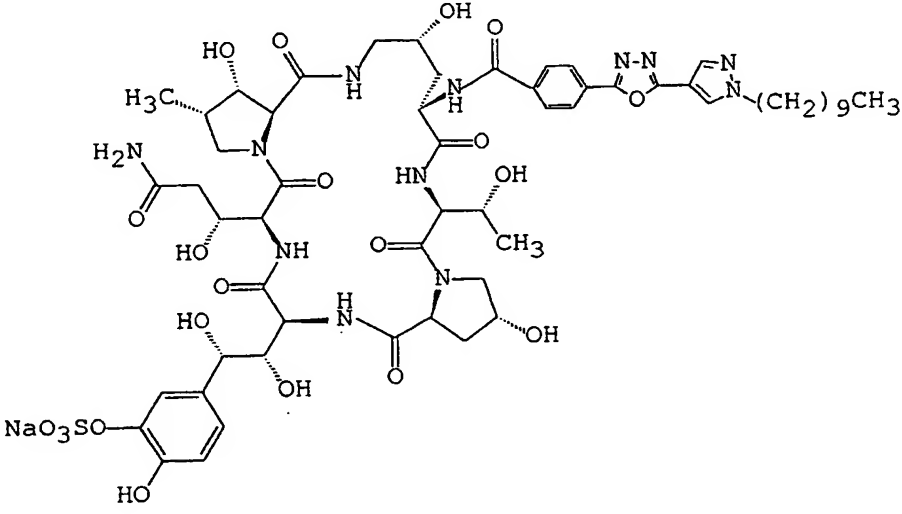
Example No.	Formula
	
39	

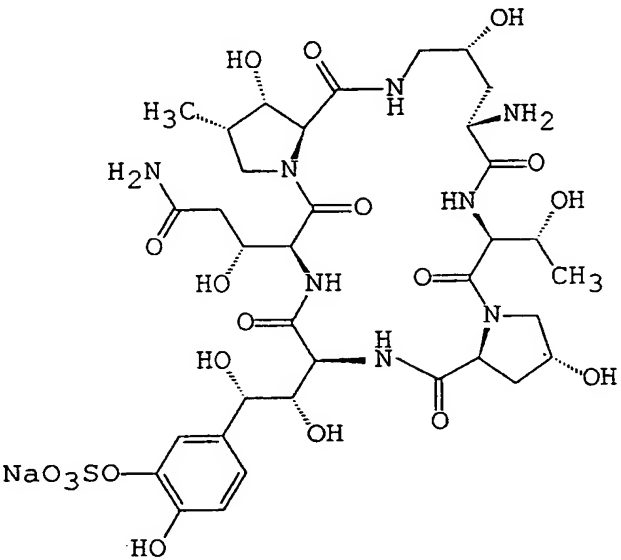
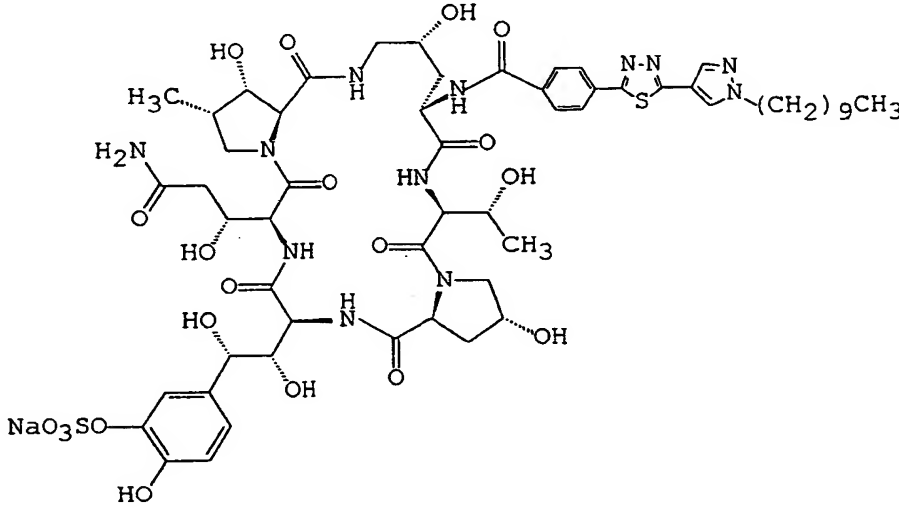
Example No.	Formula
40	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (NaO<sub>3</sub>SO-) attached to a phenyl ring, and several hydroxyl groups. The structure is highly branched and contains multiple chiral centers.</p>
	 <p>The chemical structure is a complex molecule, similar to the one above, but with a different side chain. It features a sodium sulfonate group (NaO<sub>3</sub>SO-) attached to a phenyl ring, and a long alkoxy chain (O(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>) attached to a phenyl ring. The structure is highly branched and contains multiple chiral centers.</p>

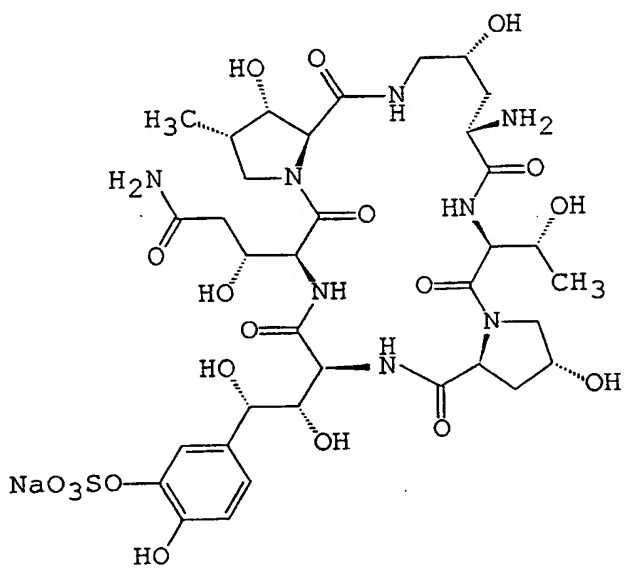
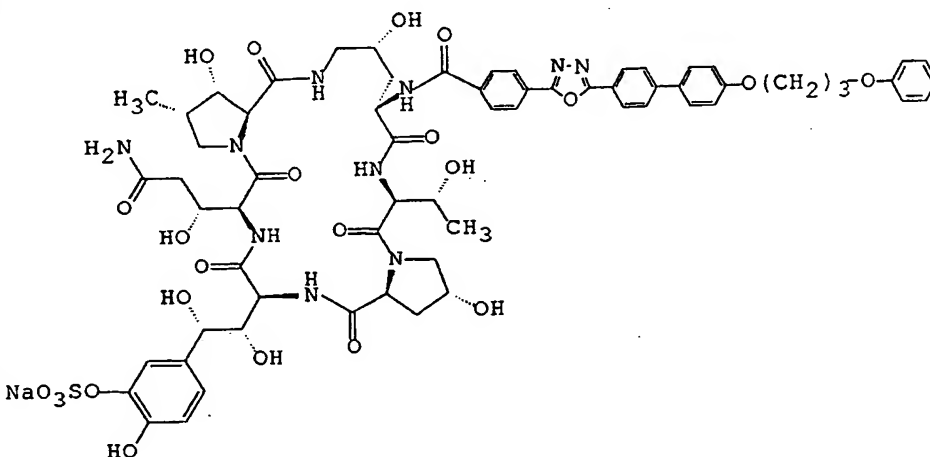


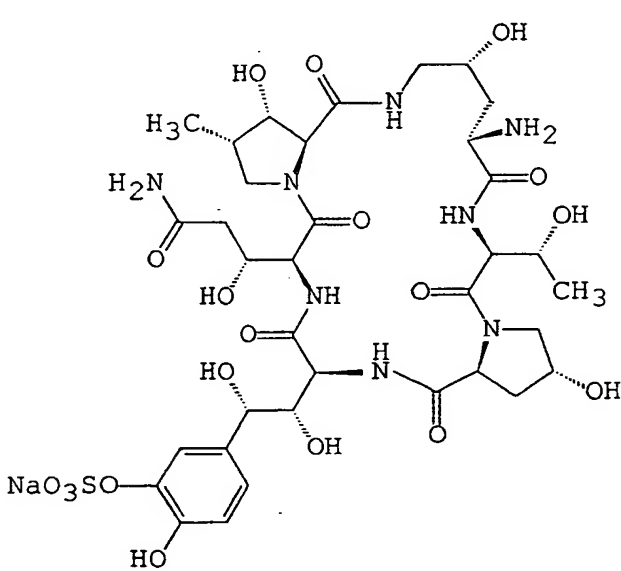
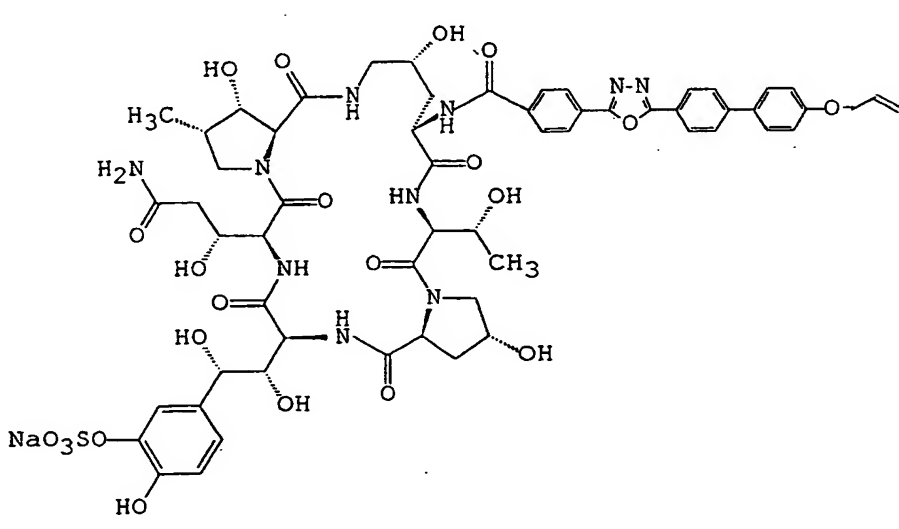
Example No.	Formula
	
41	

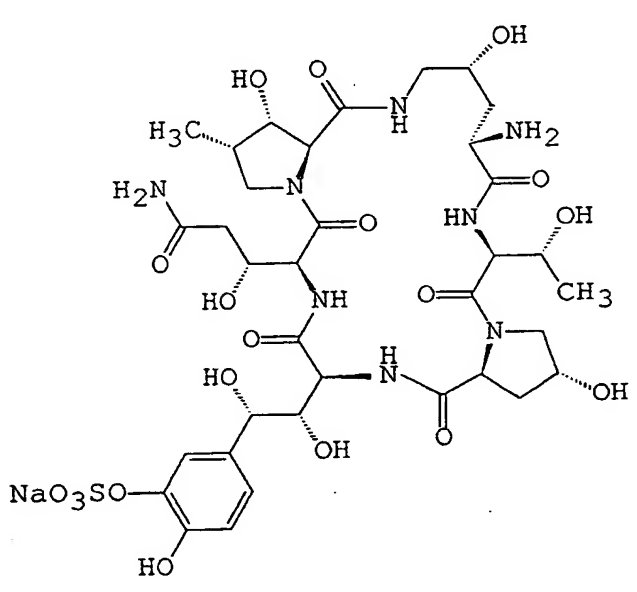
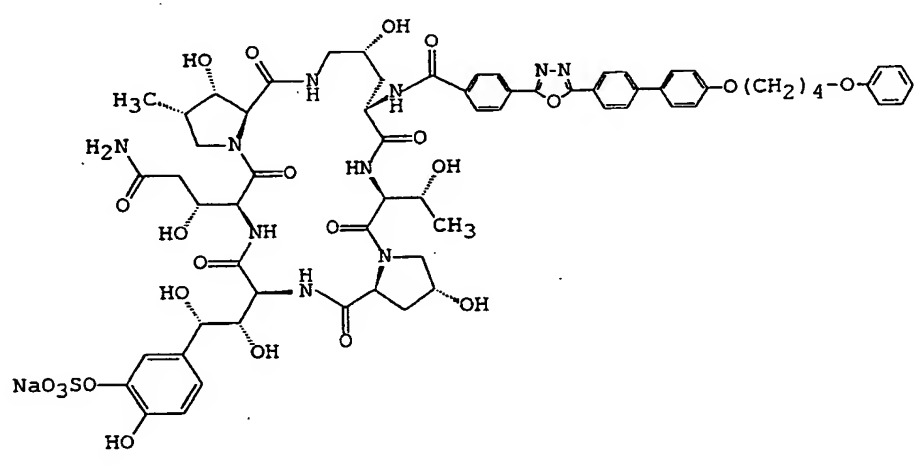
Example No.	Formula
	 <p>Chemical structure of a complex molecule, likely a derivative of a natural product. It features a central core with multiple fused and linked rings, including a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
42	 <p>Chemical structure of a complex molecule, likely a derivative of a natural product. It features a central core with multiple fused and linked rings, including a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>

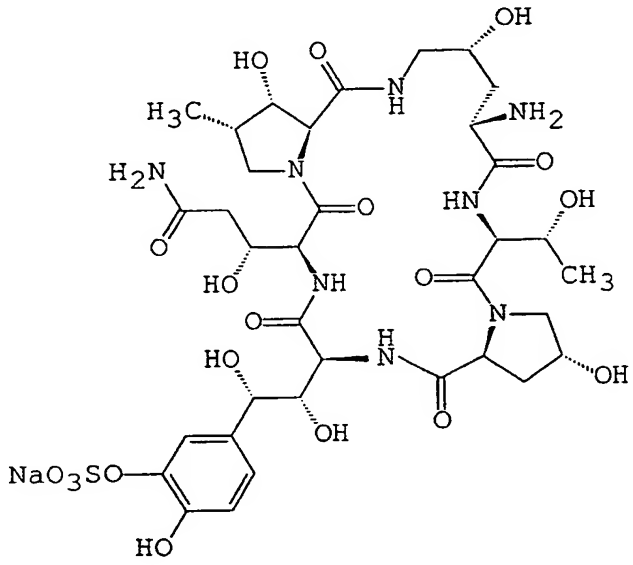
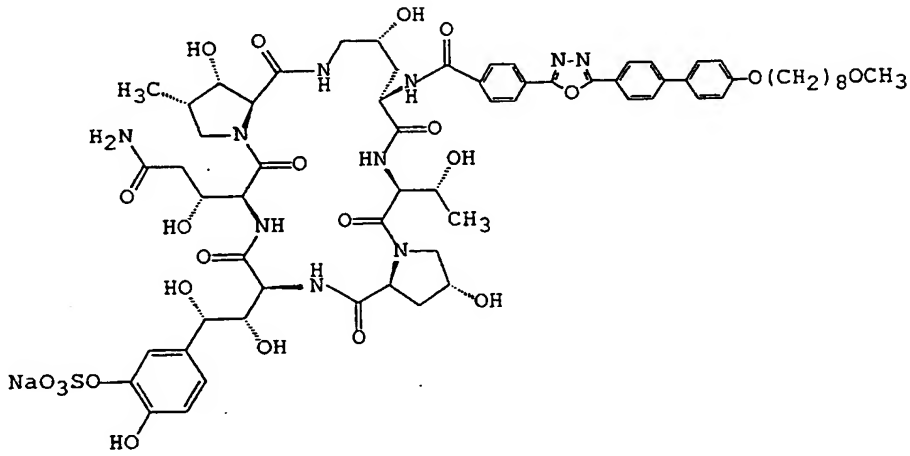
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
43	 <p>The structure is similar to the one above, but with a different side chain. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The side chain includes a long alkyl chain (CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub> and a pyrazole ring system.</p>

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide and ester linkages. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several chiral centers.</p>
44	 <p>This structure is similar to the one above, but it features a different side chain. It includes a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several chiral centers. The side chain is more complex, featuring a sulfonamide group (SO<sub>2</sub>NH-) and a long alkyl chain (CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>.</p>

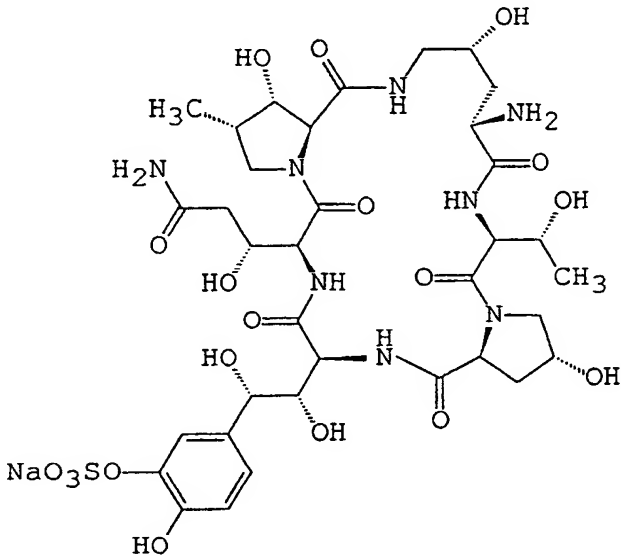
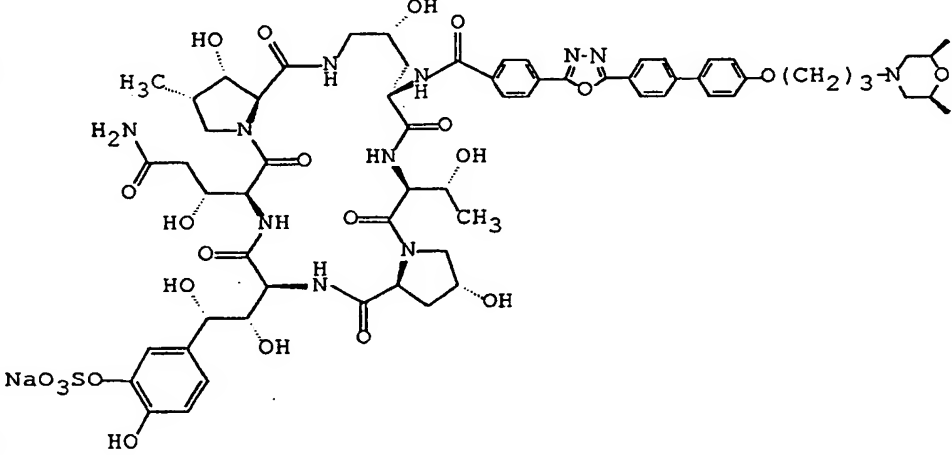
Example. No.	Formula
45	 <p>The structure shows a complex molecule with a central core. It features a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The molecule also contains several amide bonds, hydroxyl groups, and a methyl group (<math>\text{H}_3\text{C}</math>).</p>
	 <p>The structure shows a complex molecule with a central core. It features a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The molecule also contains several amide bonds, hydroxyl groups, and a methyl group (<math>\text{H}_3\text{C}</math>).</p>

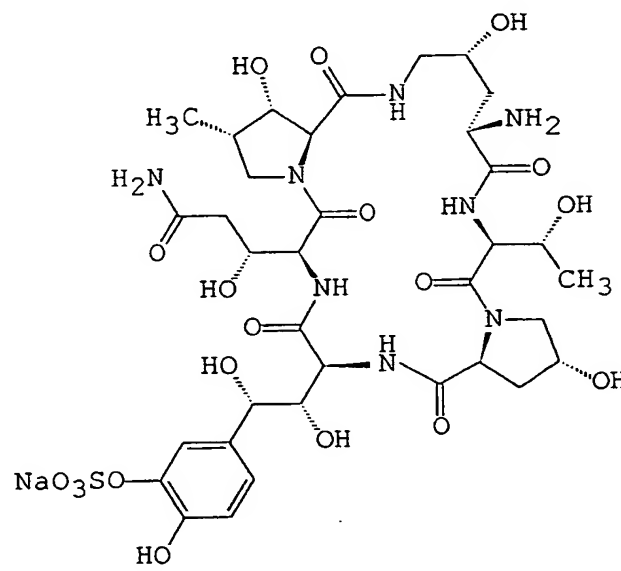
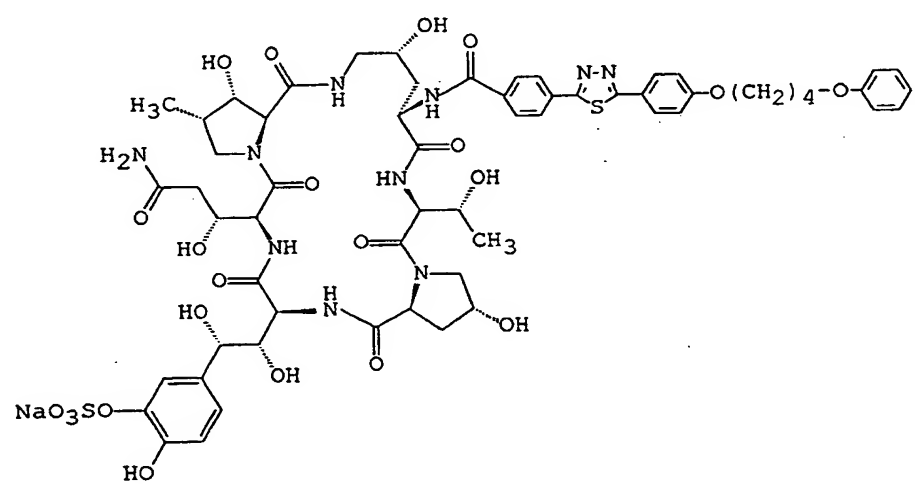
Example No.	Formula
	
46	

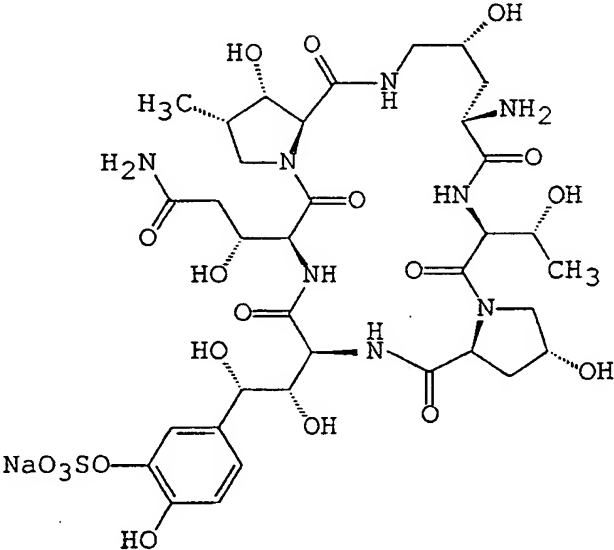
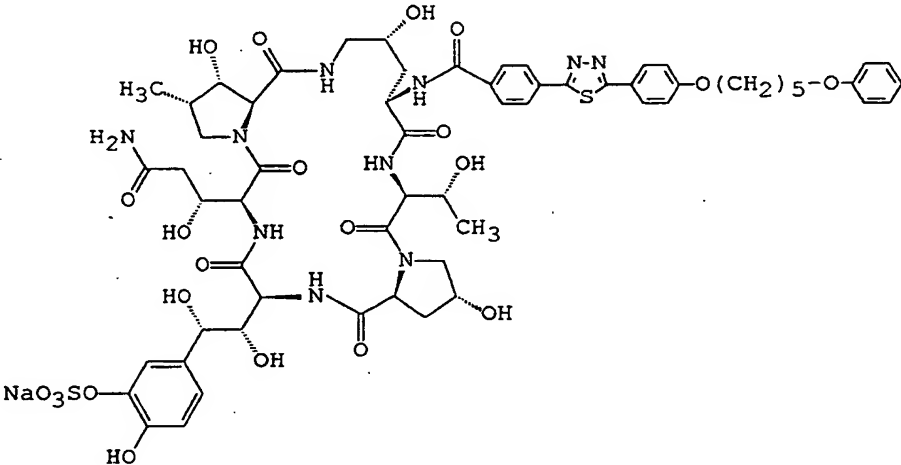
Example No.	Formula
	
47	

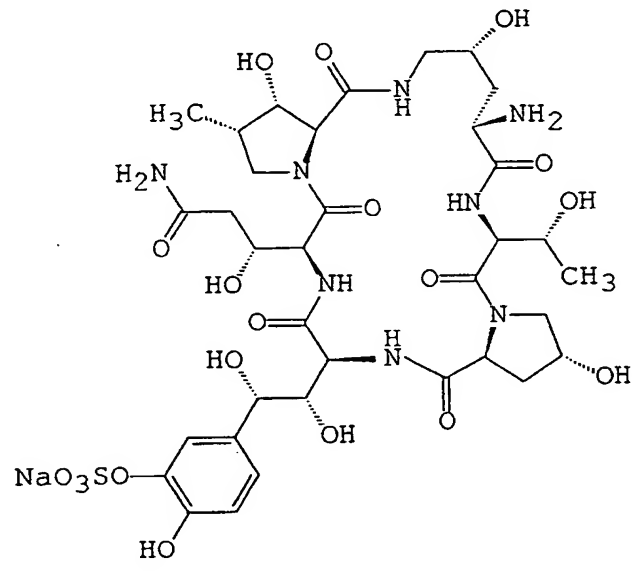
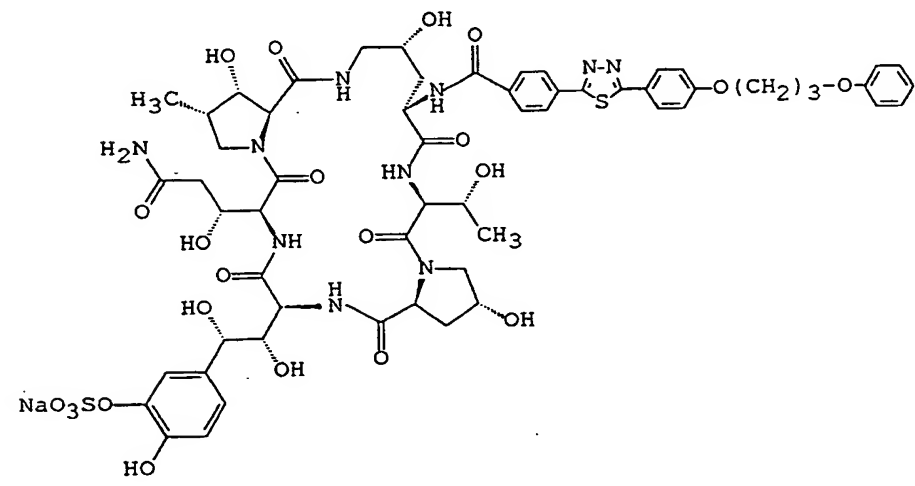
Example No.	Formula
	
48	

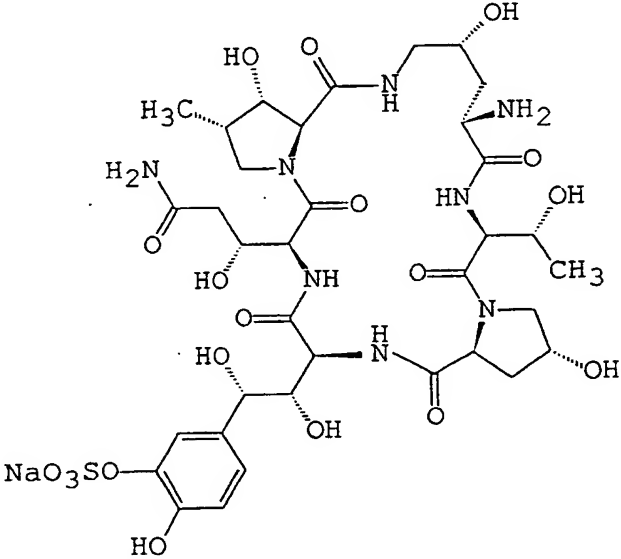
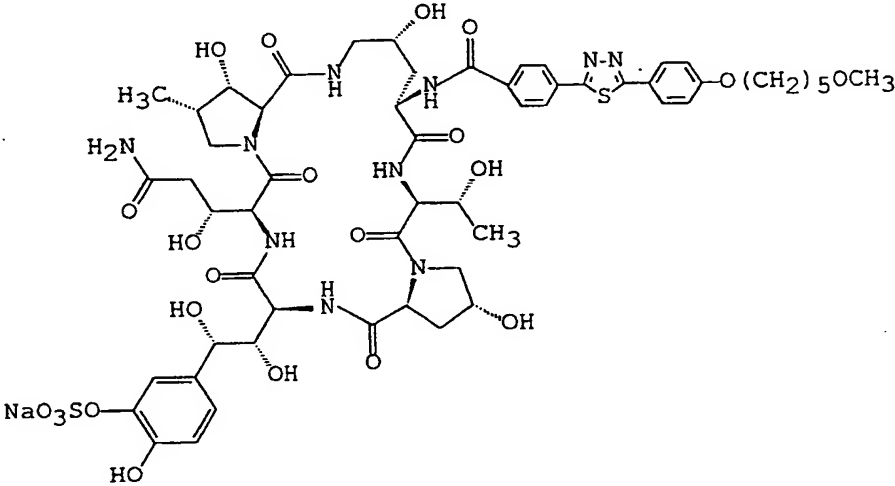


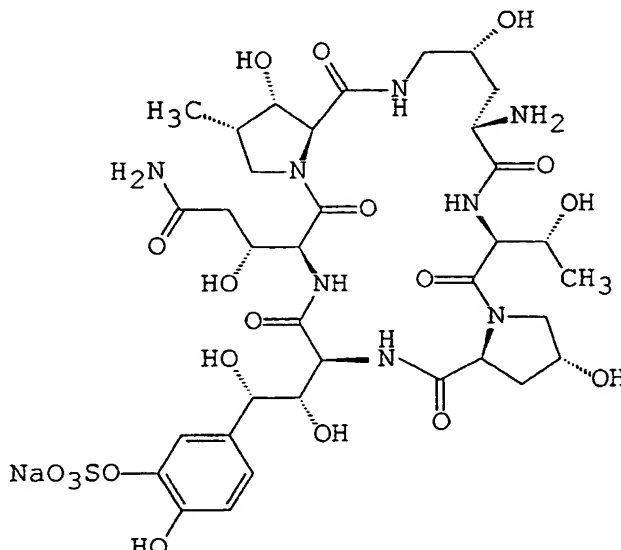
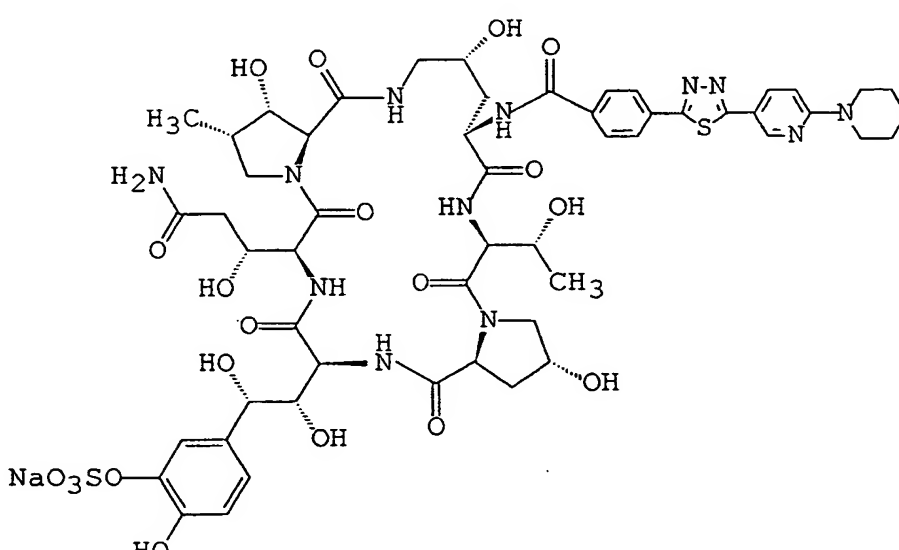
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide and hydroxyl groups. It features a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a 4-hydroxyphenyl group. The molecule is composed of several interconnected rings and chains, including a central amide linkage and various hydroxyl and methyl substituents.</p>
49	 <p>This structure is similar to the one in the first row, but it features a different side chain. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a 4-hydroxyphenyl group. The side chain is more complex, involving a long chain with a methoxy group and a 4-methoxyphenyl group at the end.</p>

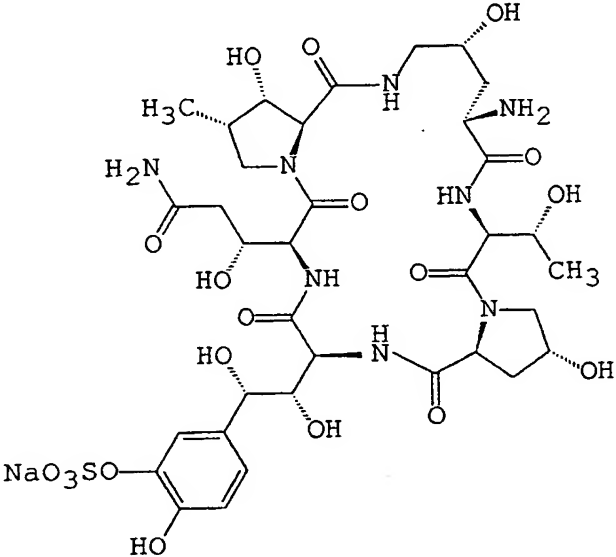
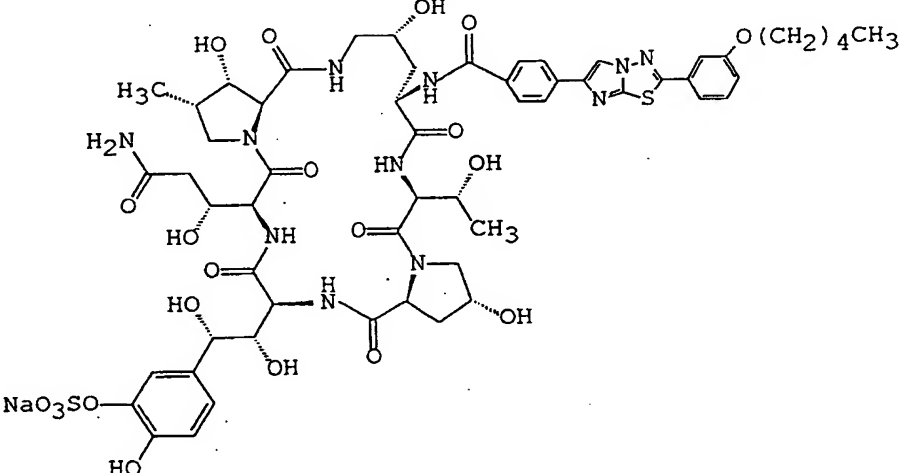
Example No.	Formula
50	 <p>The structure shows a complex polycyclic molecule. It features a central core with several fused and linked rings, including a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a 4-hydroxyphenyl group. The molecule contains multiple hydroxyl groups, amide bonds, and a methyl group.</p>
	 <p>This structure is similar to the one above but features a different side chain. It includes a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a 4-hydroxyphenyl group. The side chain contains a sulfonamide group, a phenyl ring, and a long alkyl chain ending in a phenyl group.</p>

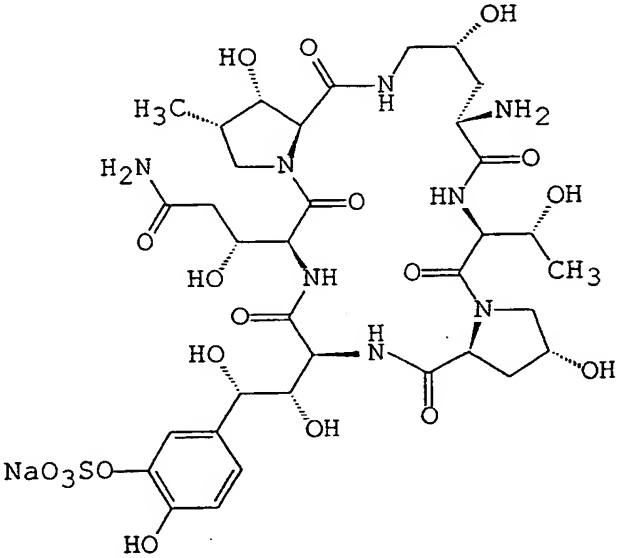
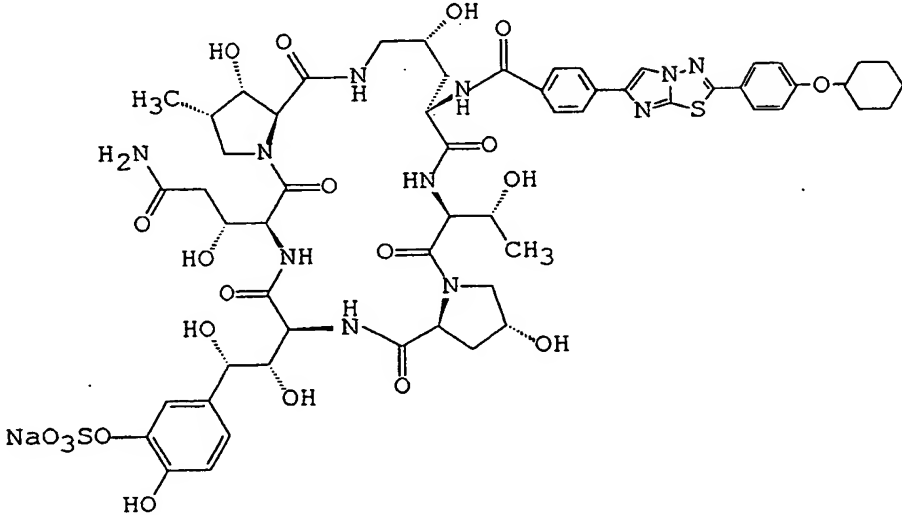
Example No.	Formula
	
51	

Example No.	Formula
	
52	

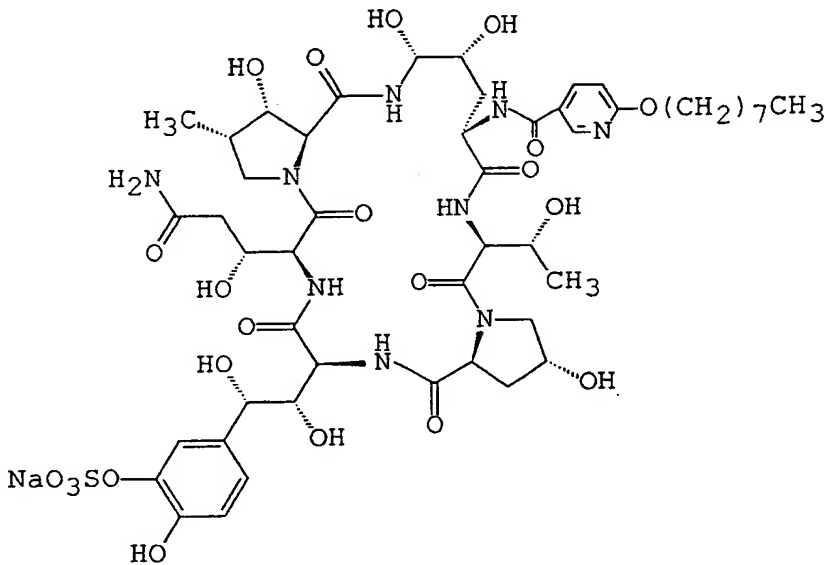
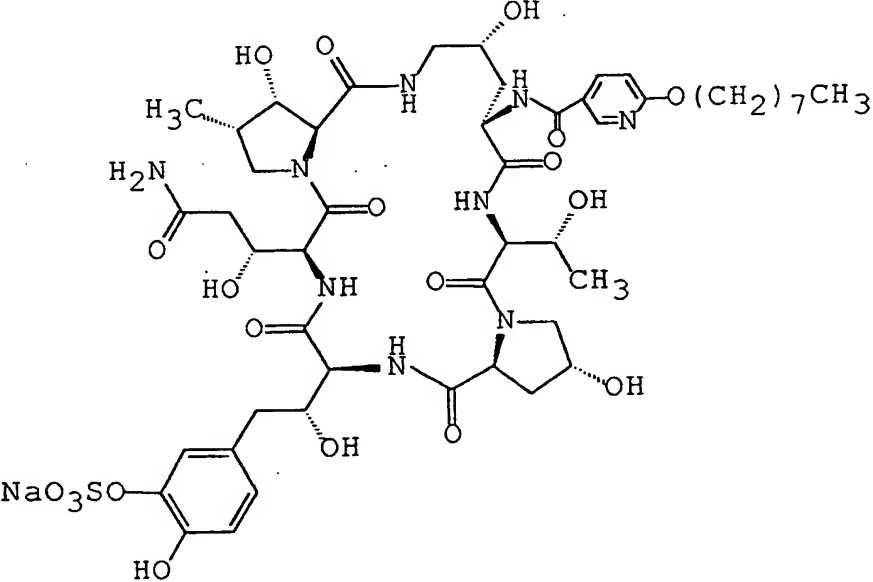
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
53	 <p>The structure is similar to the one above, but with a different side chain. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The side chain includes a thiazole ring and a long alkyl chain (CH<sub>2</sub>)<sub>5</sub>OCH<sub>3</sub>.</p>

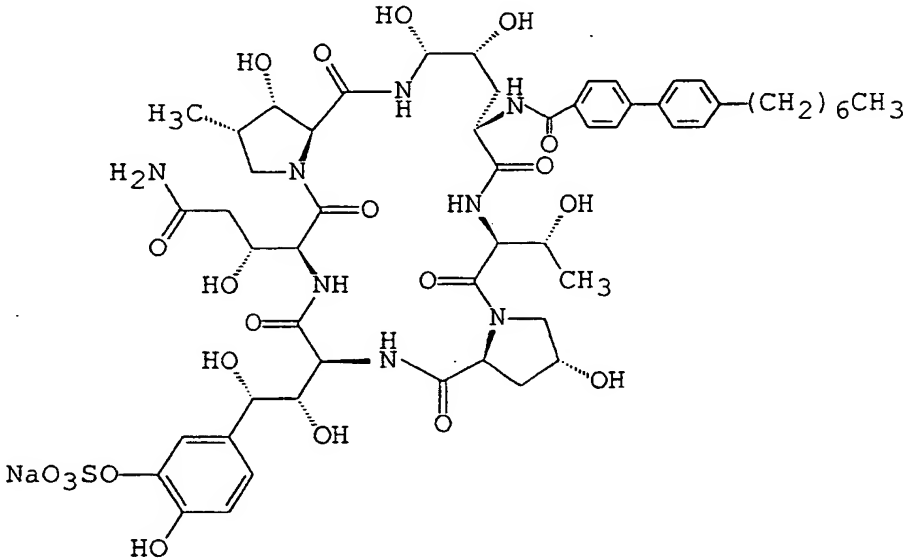
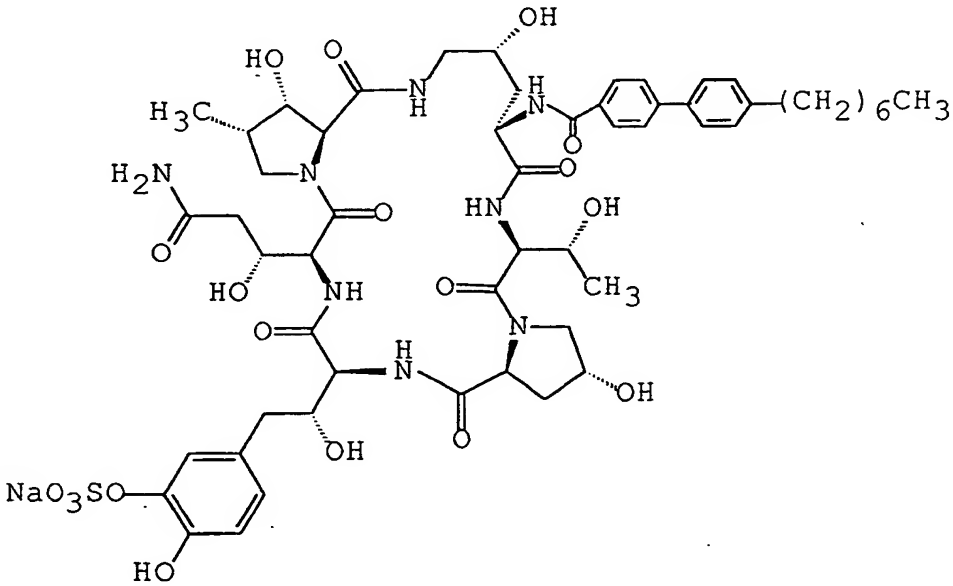
Example No.	Formula
	
54	

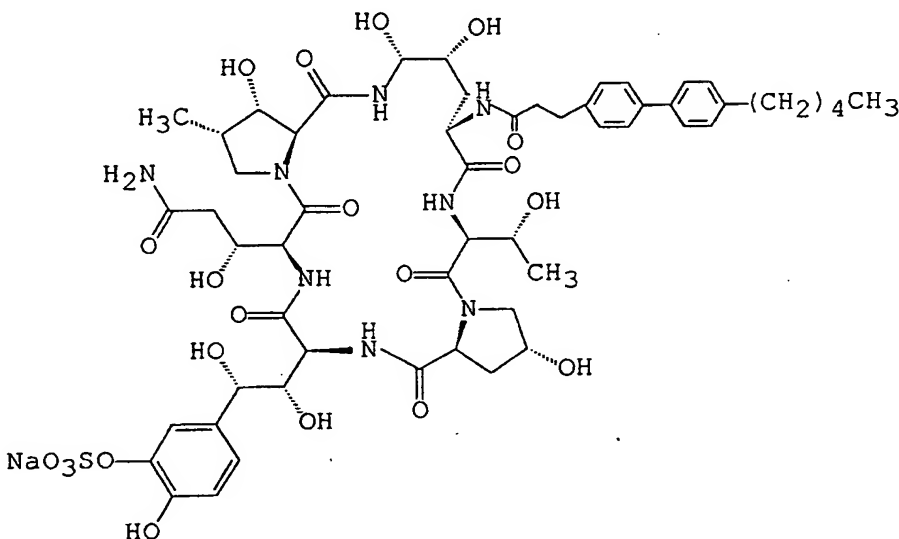
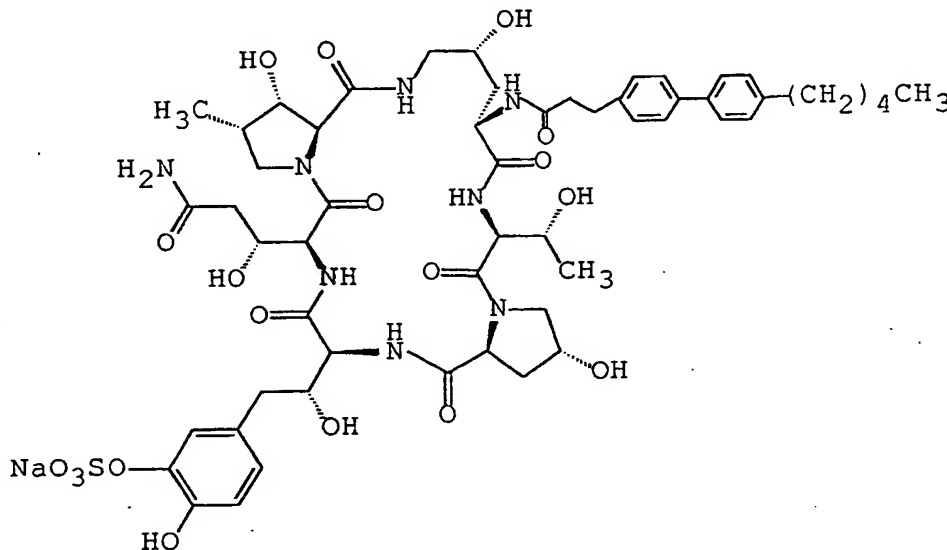
Example No.	Formula
55	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
	 <p>The chemical structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The structure is highly branched and contains several chiral centers indicated by wedged and dashed bonds. It also features a long alkoxy chain (<math>\text{O}(\text{CH}_2)_4\text{CH}_3</math>) and a thiazole ring system.</p>

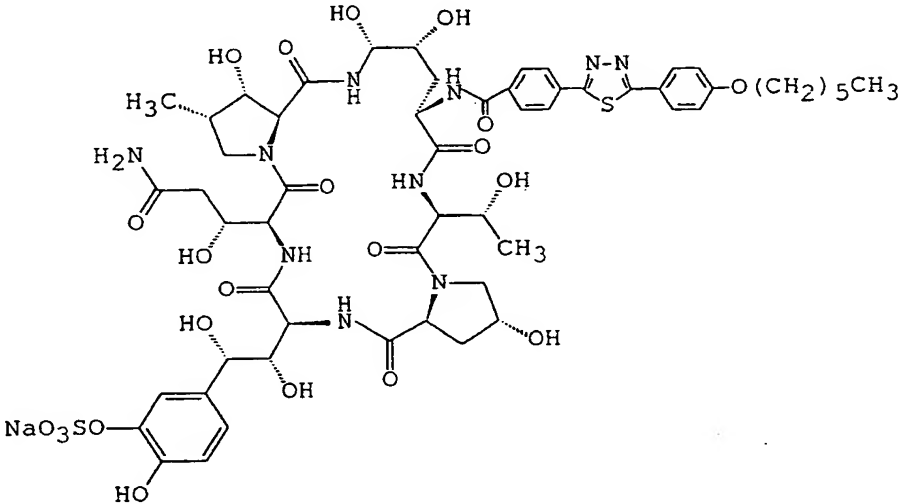
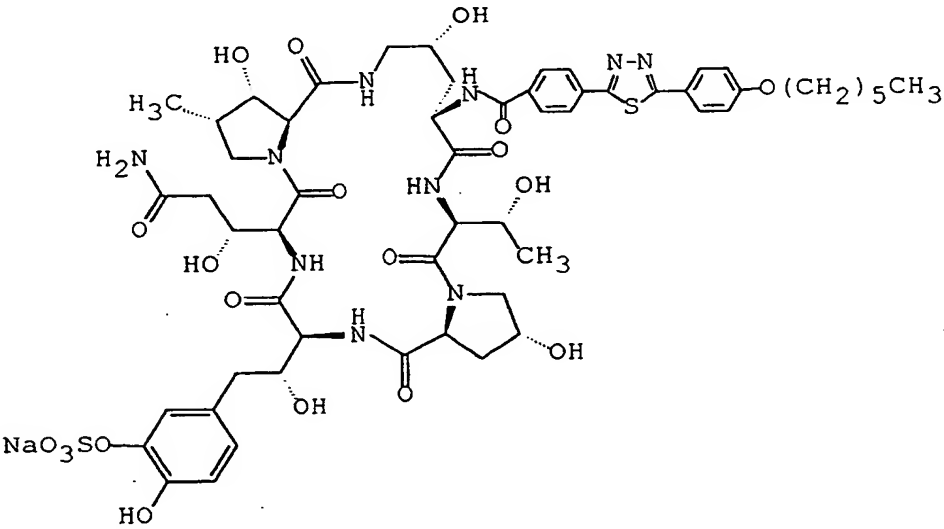
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
56	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>

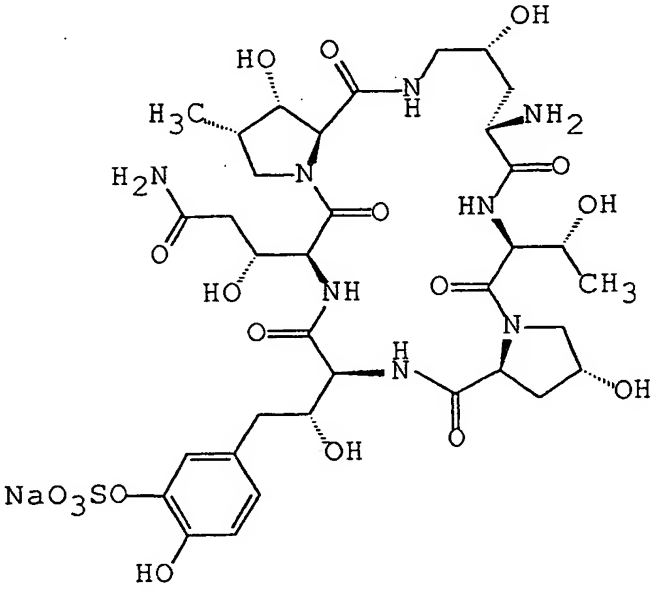
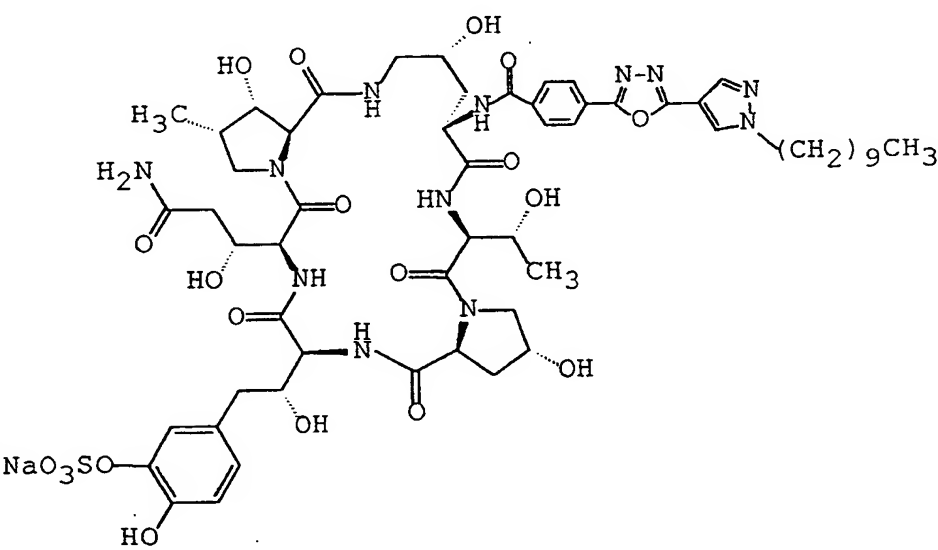


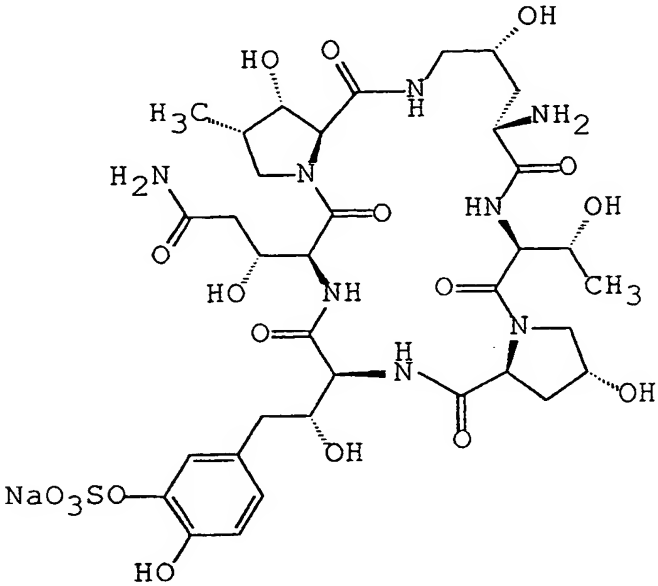
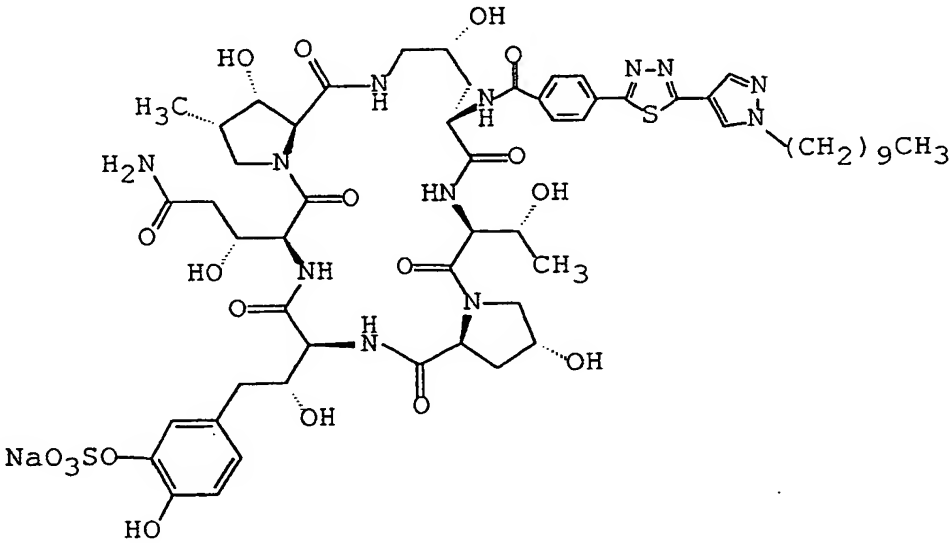
Example No.	Formula
	
57	

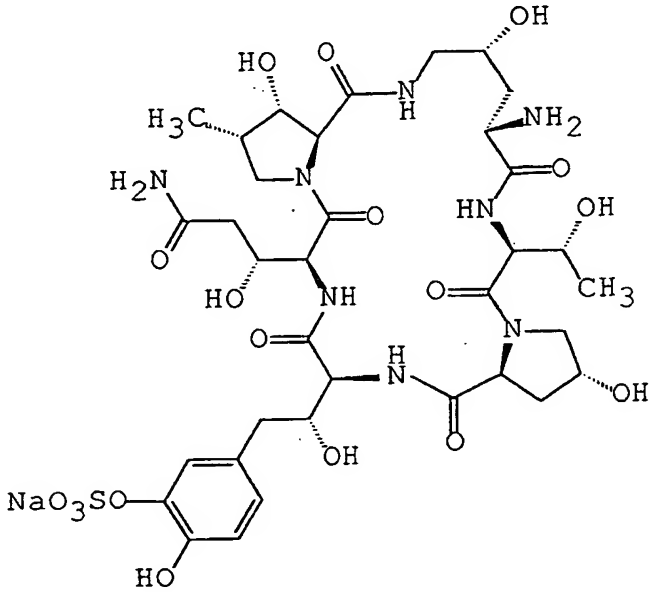
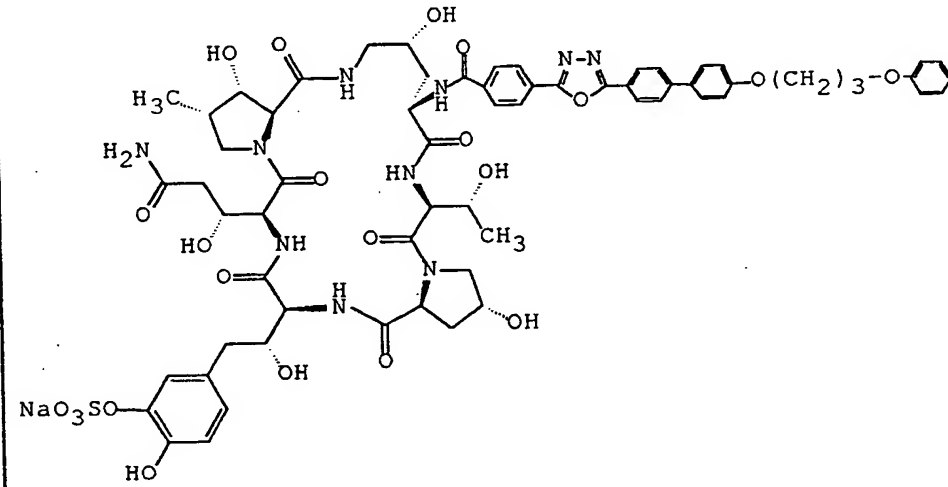
Example No.	Formula
	
58	

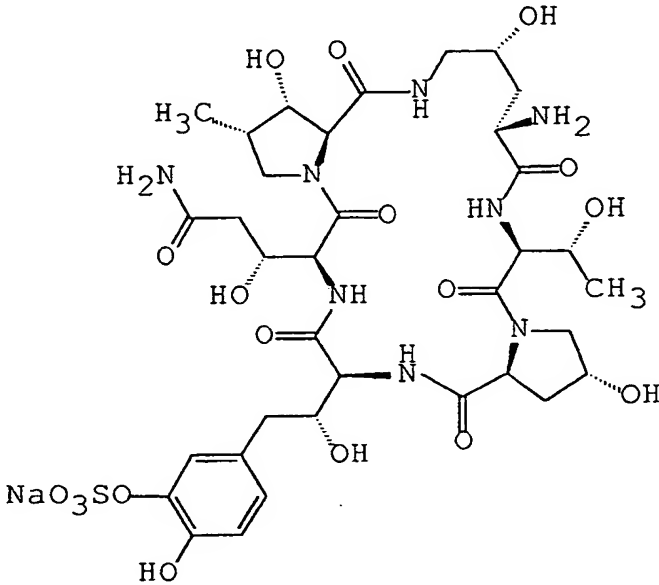
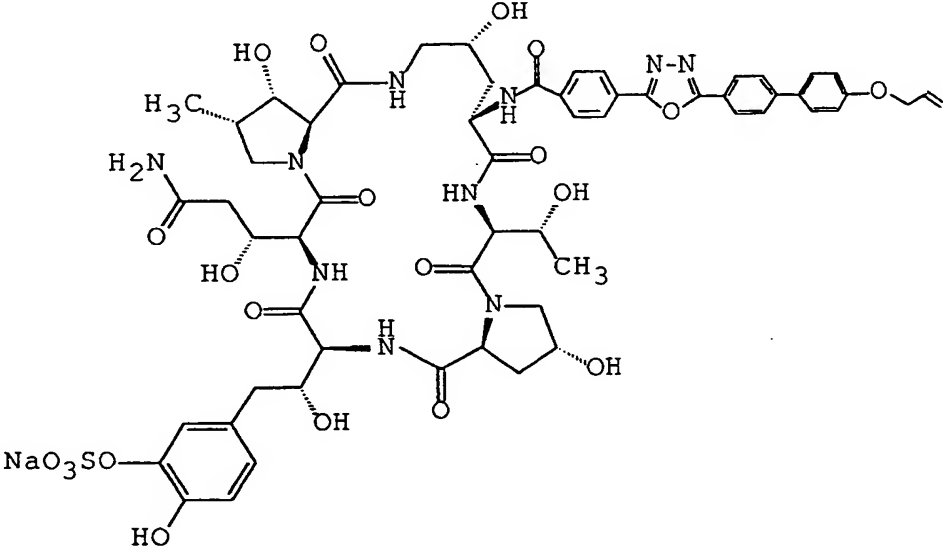
Example No.	Formula
	
59	

Example No.	Formula
	
60	

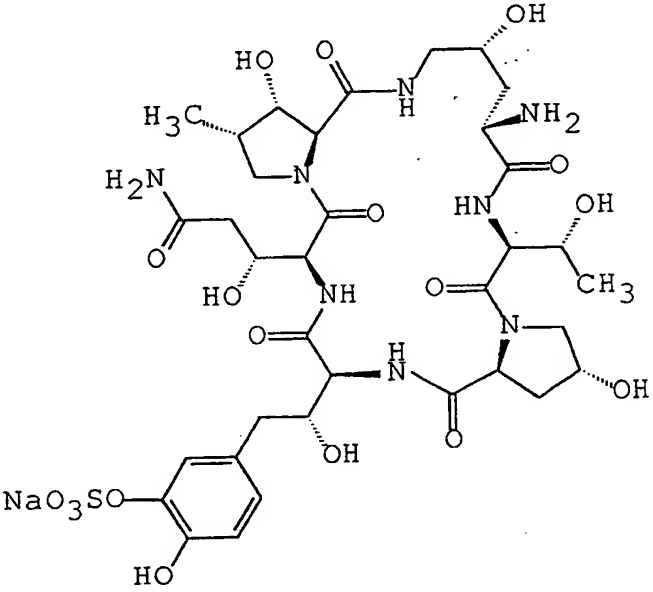
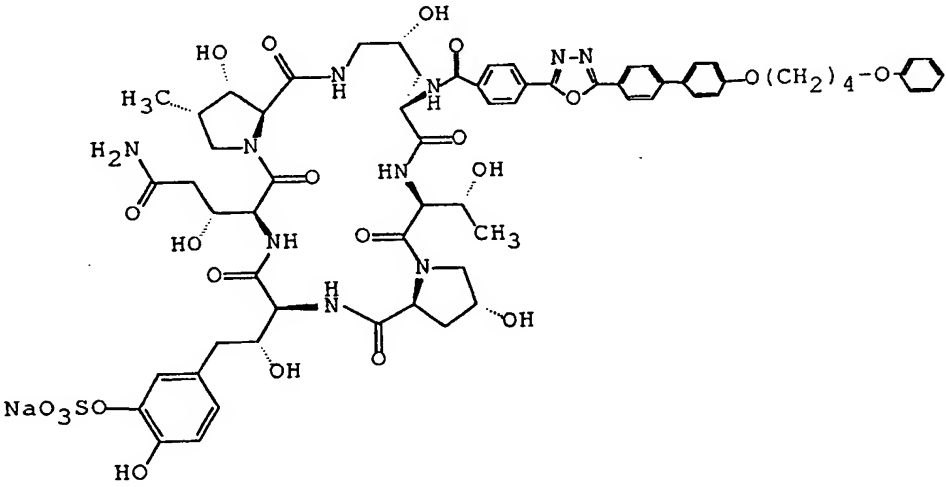
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
61	 <p>The structure is similar to the one above, but with a different side chain. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The side chain includes a pyrazole ring and a long alkyl chain (CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>.</p>

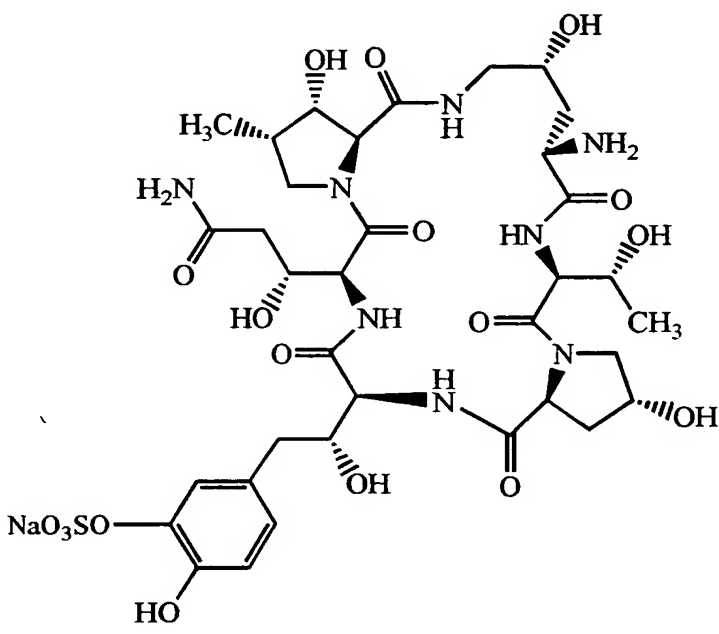
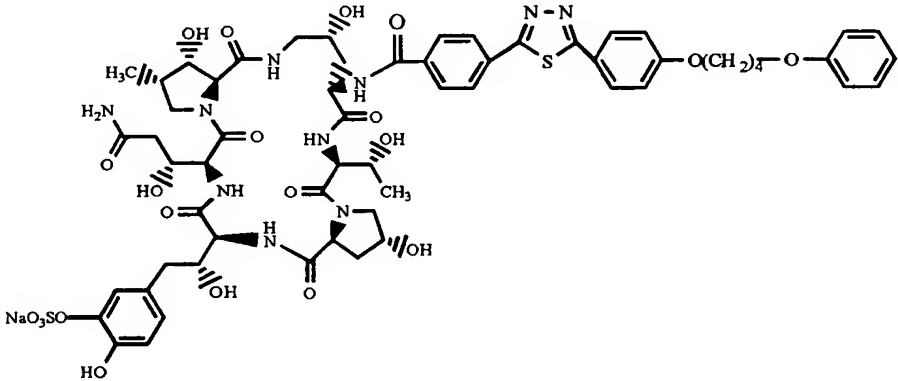
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide bonds, hydroxyl groups, and a sodium sulfonate group. It features a central chain with several side chains, including a methyl group, a hydroxyl group, and a sodium sulfonate group. The molecule is highly branched and contains several chiral centers.</p>
62	 <p>This structure is similar to the one above, but it features a different side chain. It includes a sodium sulfonate group, a hydroxyl group, and a long alkyl chain. The molecule is highly branched and contains several chiral centers.</p>

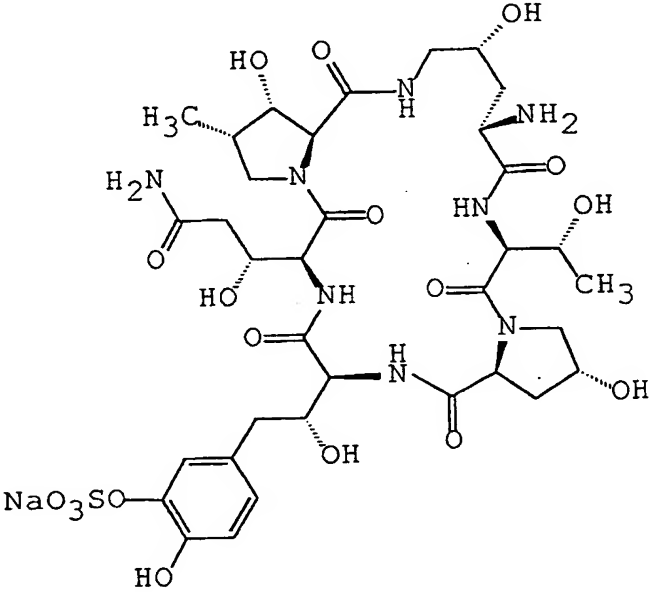
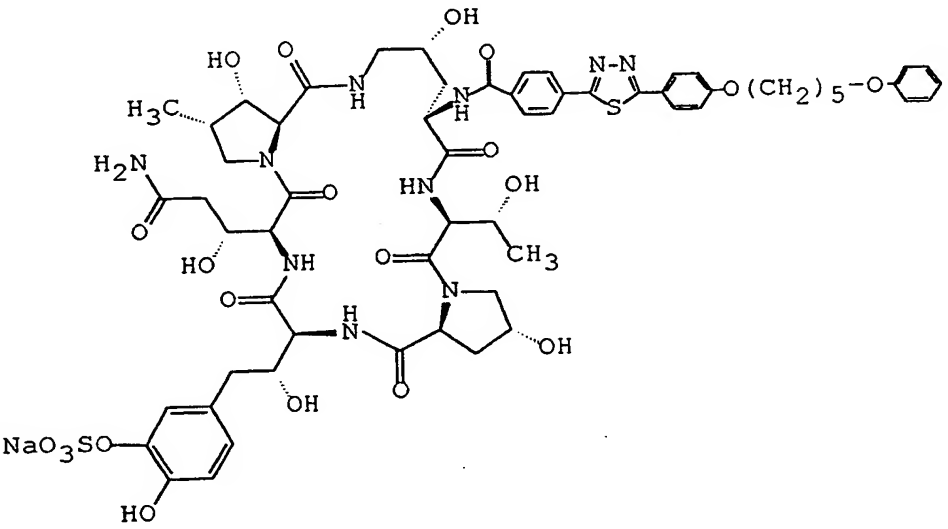
Example No.	Formula
	
63	

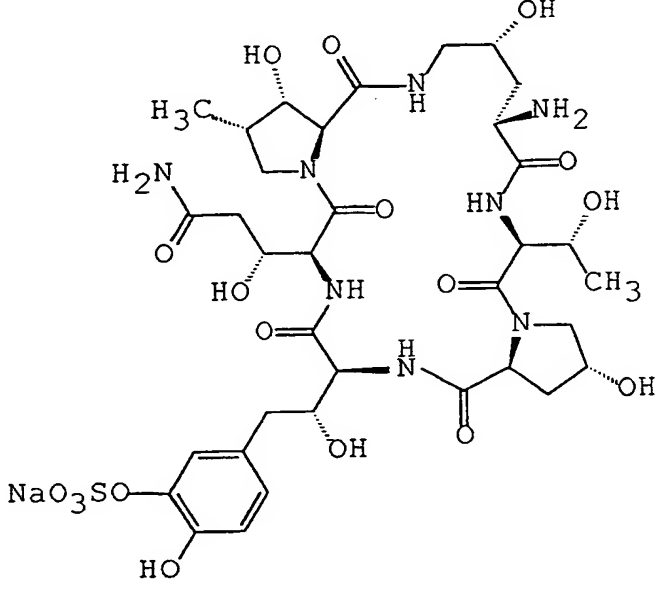
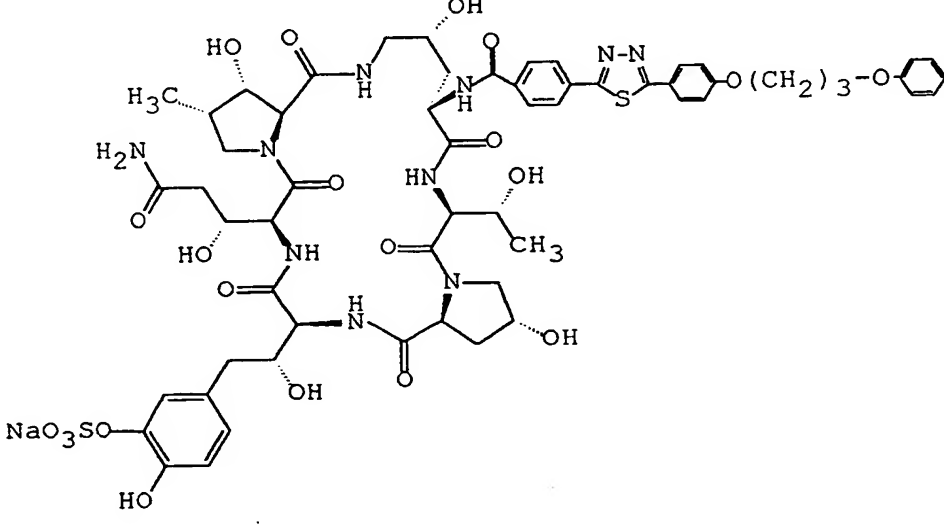
Example No.	Formula
	 <p>The structure shows a cyclic peptide derivative. It features a central core with two pyrrolidine rings and several amide bonds. A side chain includes a 4-hydroxyphenyl sodium sulfonate group (NaO<sub>3</sub>SO-C<sub>6</sub>H<sub>4</sub>-OH) attached to a hydroxymethyl group. Other substituents include a methyl group, a hydroxyl group, and an amino group.</p>
64	 <p>The structure shows a cyclic peptide derivative similar to the one above, but with a more complex side chain. It includes a 4-hydroxyphenyl sodium sulfonate group (NaO<sub>3</sub>SO-C<sub>6</sub>H<sub>4</sub>-OH) and a long chain containing a diazo group (N=N) and a terminal allyl ether group (-O-CH<sub>2</sub>-CH=CH<sub>2</sub>).</p>

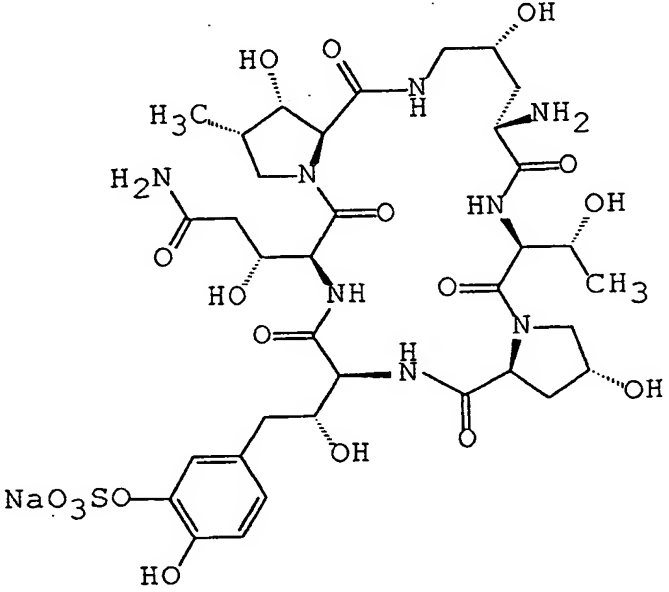
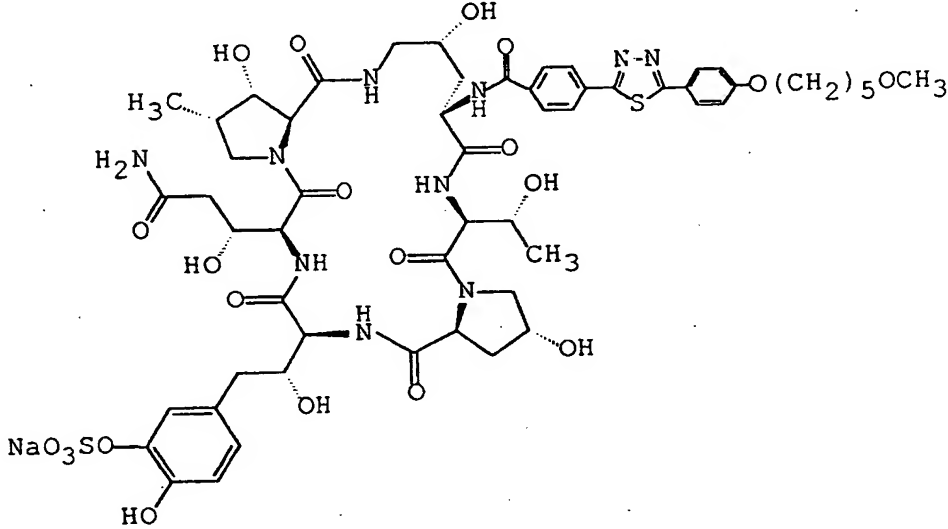


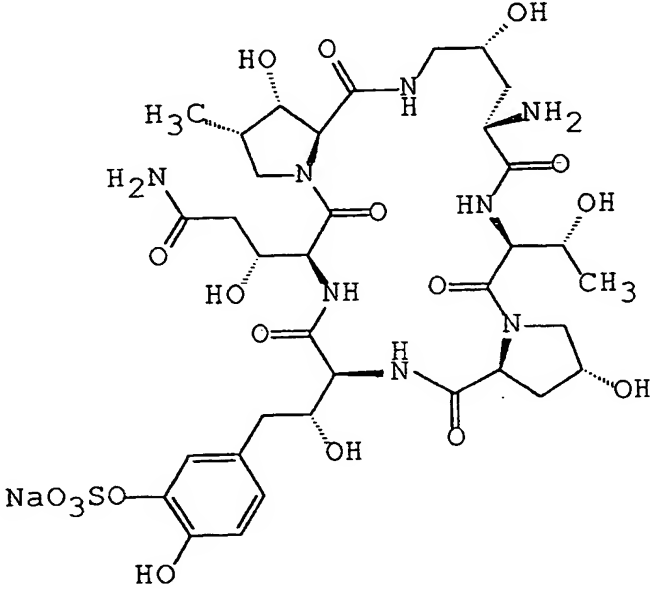
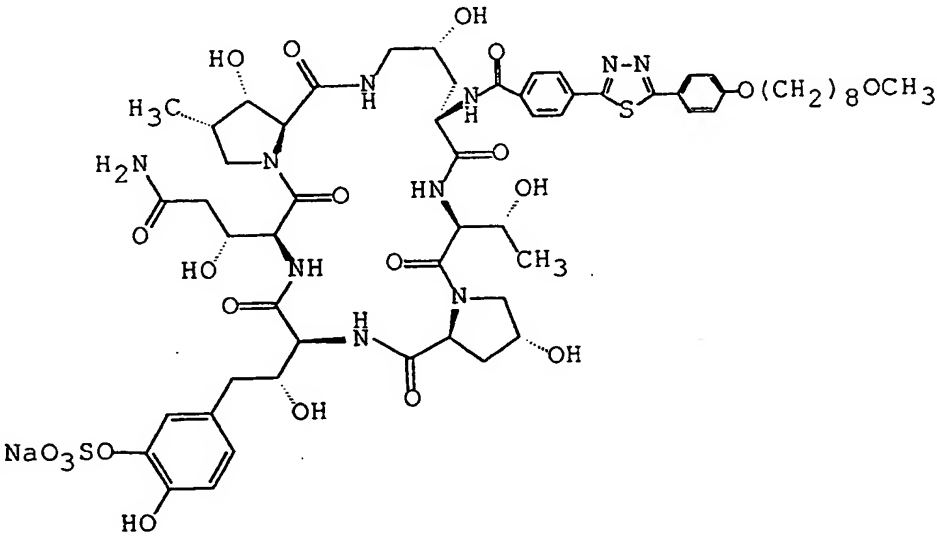
Example No.	Formula
	
65	

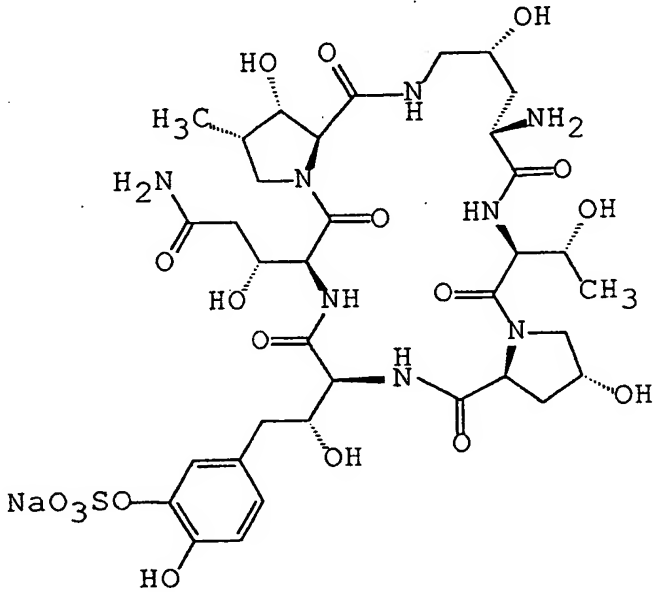
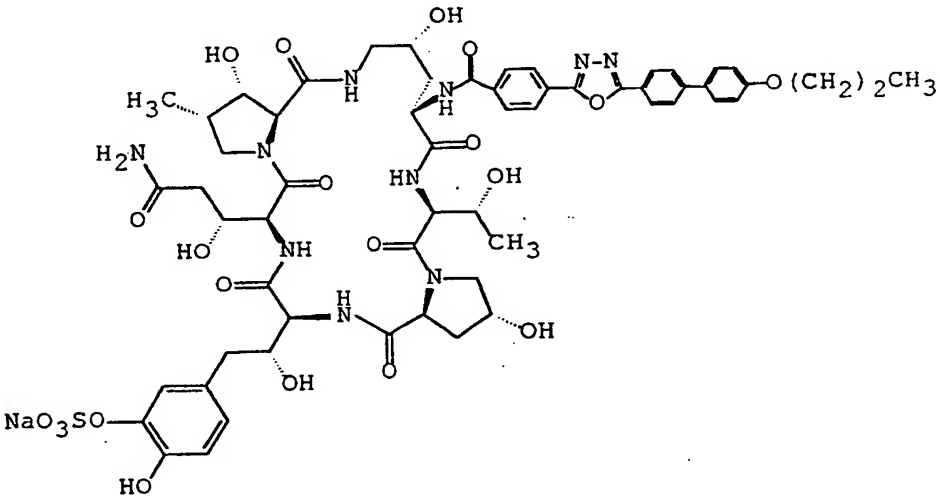
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfonatophenyl group. It features a central amide linkage connecting two fragments. One fragment includes a 4-hydroxy-3-sulfonatophenyl group (NaO<sub>3</sub>SO- and HO- substituents) and a hydroxyl group. The other fragment includes a methyl group, a hydroxyl group, and an amide bond. The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
66	 <p>This structure is similar to the one above but features a different side chain. It includes a 4-hydroxy-3-sulfonatophenyl group (NaO<sub>3</sub>SO- and HO- substituents) and a hydroxyl group. The side chain is more complex, featuring a hydroxyl group, an amide bond, and a 4-hydroxy-3-sulfonatophenyl group. The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide bonds, hydroxyl groups, and a sodium sulfonate group. It features a central chain with several side chains, including a methyl group, a hydroxyl group, and a sodium sulfonate group. The molecule is highly branched and contains several chiral centers.</p>
67	 <p>The structure shows a complex molecule with multiple amide bonds, hydroxyl groups, and a long alkoxy chain. It features a central chain with several side chains, including a methyl group, a hydroxyl group, and a long alkoxy chain. The molecule is highly branched and contains several chiral centers.</p>

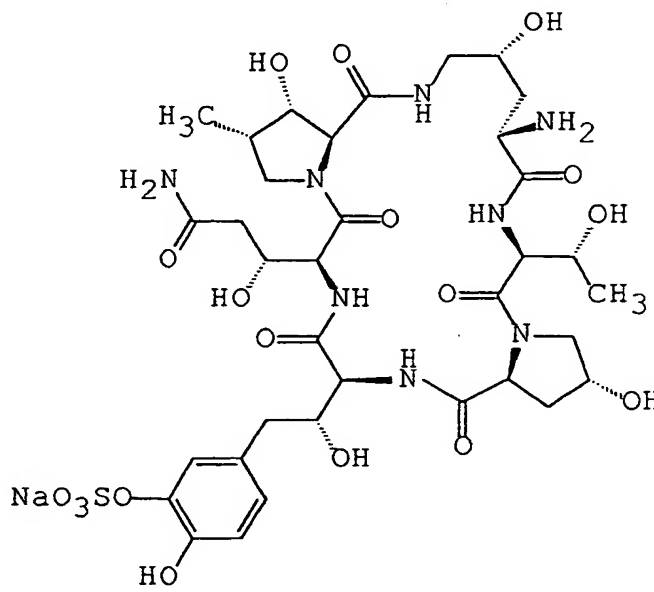
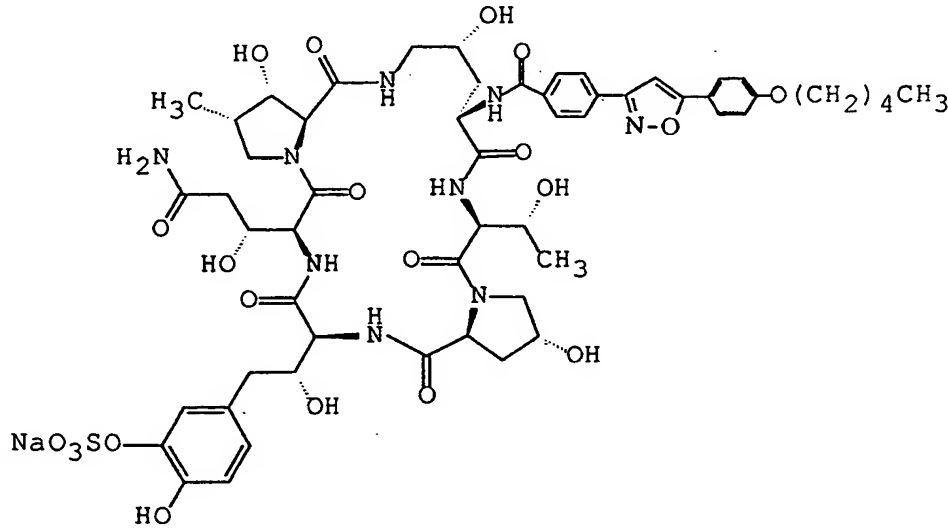
Example No.	Formula
	 <p>The structure is a complex molecule featuring a central core with multiple amide and ester linkages. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. Other functional groups include a methyl group (<math>\text{H}_3\text{C}</math>), a hydroxyl group (<math>\text{OH}</math>), and a carboxamide group (<math>\text{H}_2\text{N}</math>).</p>
68	 <p>This structure is similar to the one above, but it features a different side chain. It includes a sodium sulfonate group (<math>\text{NaO}_3\text{SO}</math>) and a hydroxyl group (<math>\text{HO}</math>) on a benzene ring. The side chain contains a thiazole ring system and a long alkoxy chain (<math>(\text{CH}_2)_3\text{O}</math>) connected to a phenyl group.</p>

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central chain with several side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several nitrogen and oxygen atoms.</p>
69	 <p>The structure is similar to the one above, but with a different side chain. It features a central chain with multiple amide, ester, and hydroxyl groups. The side chain includes a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several nitrogen and oxygen atoms.</p>

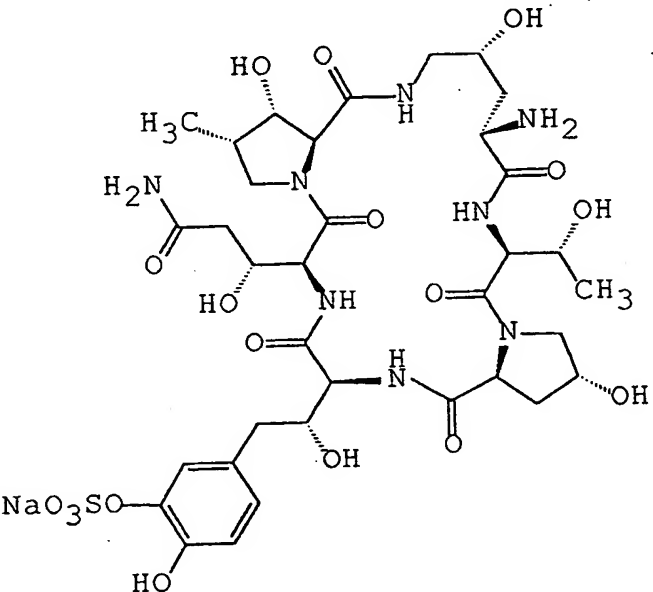
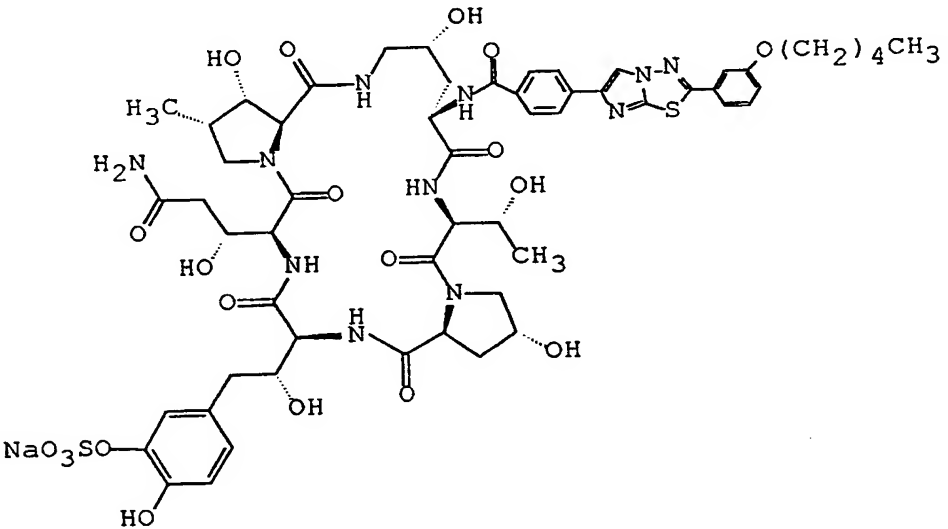
Example No.	Formula
	
70	

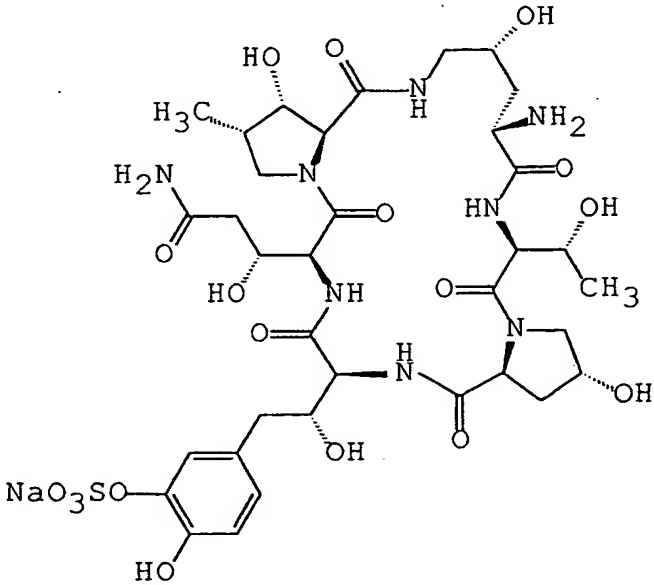
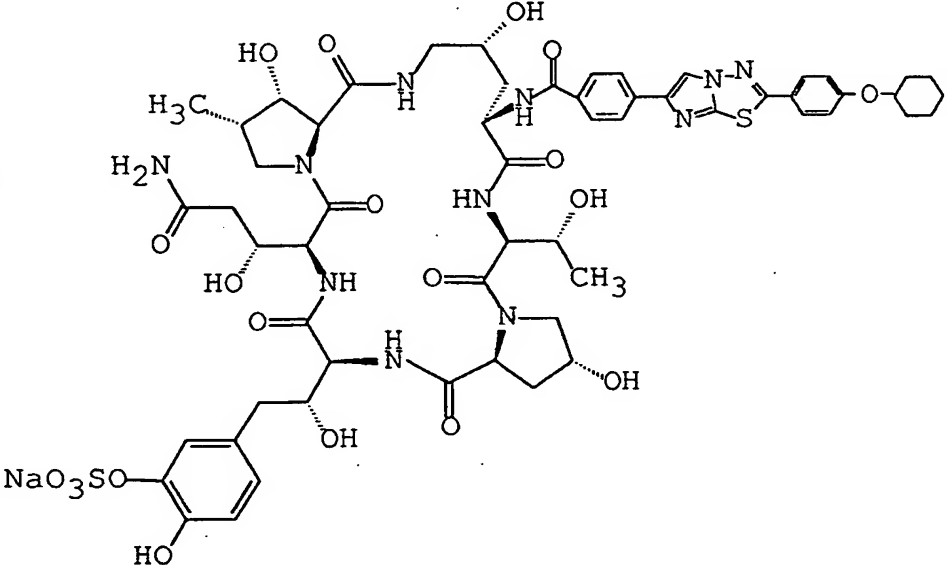
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide bonds, hydroxyl groups, and a sodium sulfonate group. It features a central chain with several side chains, including a 4-hydroxyphenyl group and a sodium sulfonate group.</p>
71	 <p>The structure is similar to the one above, but with a different side chain. It features a central chain with multiple amide bonds, hydroxyl groups, and a sodium sulfonate group. The side chain includes a 4-hydroxyphenyl group and a sodium sulfonate group, and is connected to a long alkyl chain via an ether linkage.</p>

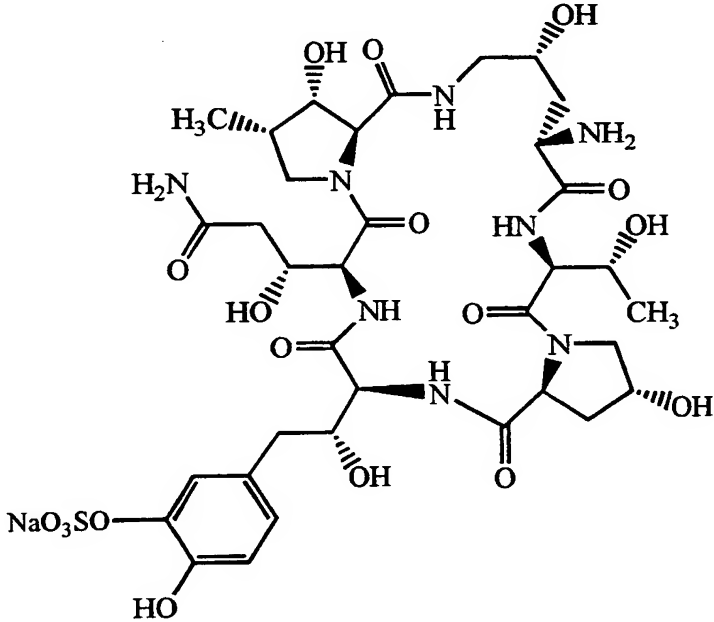
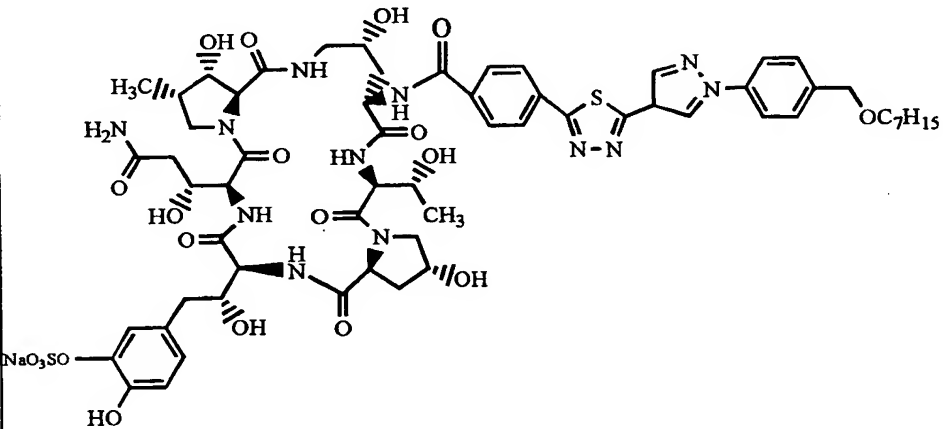
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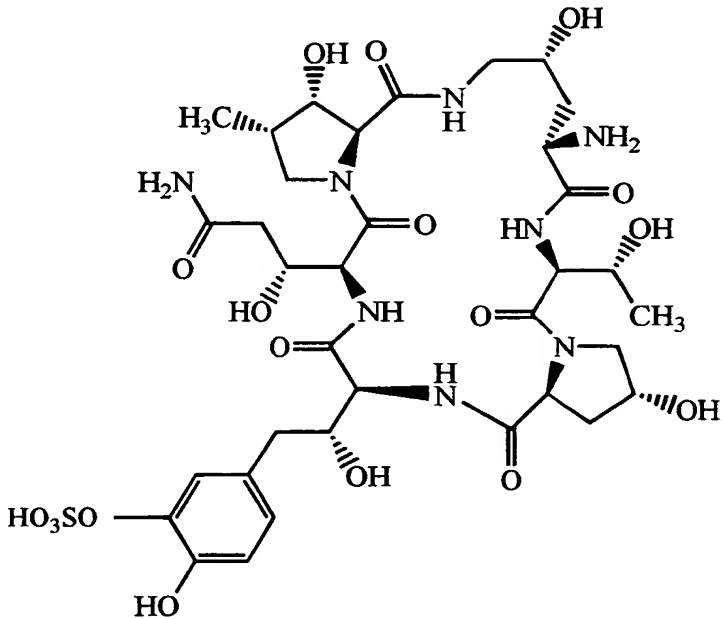
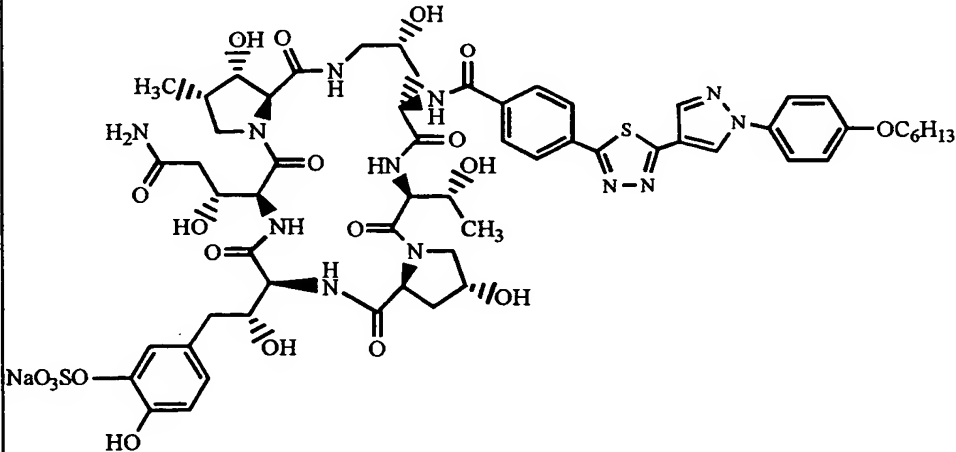
Example No.	Formula
	
72	

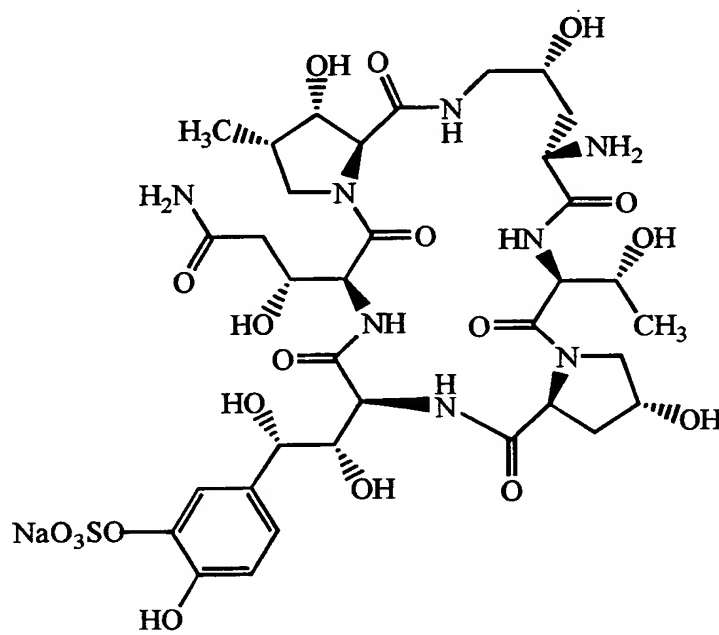
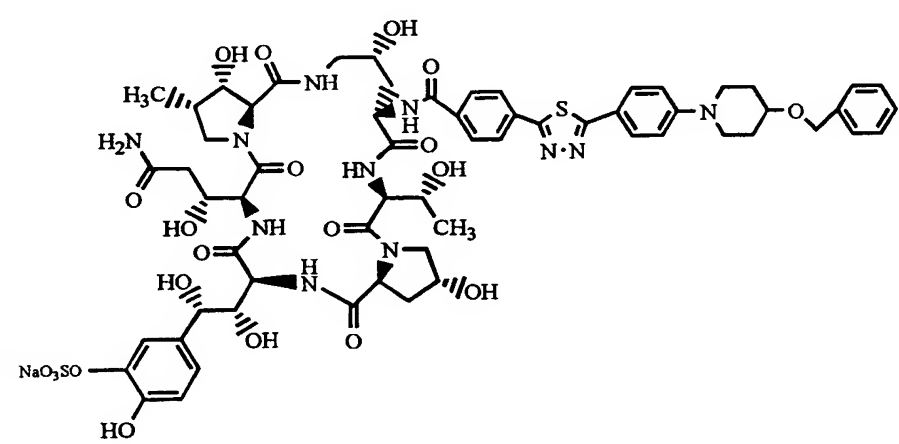


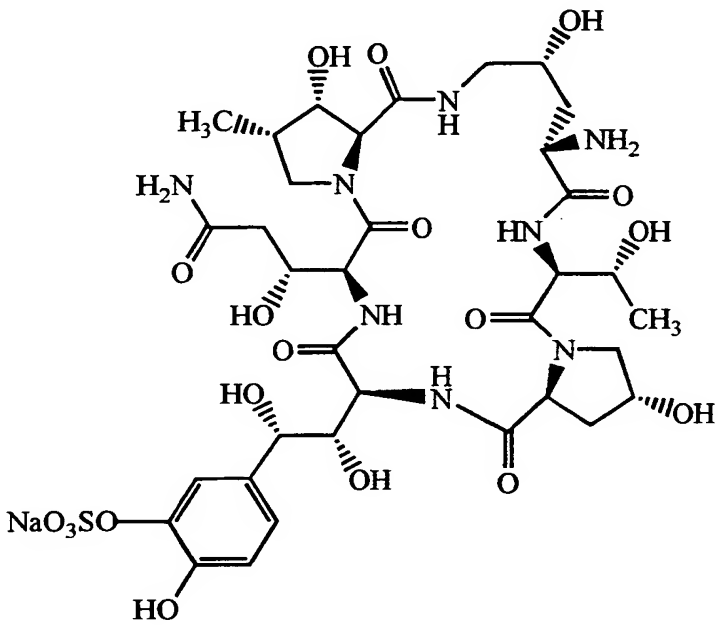
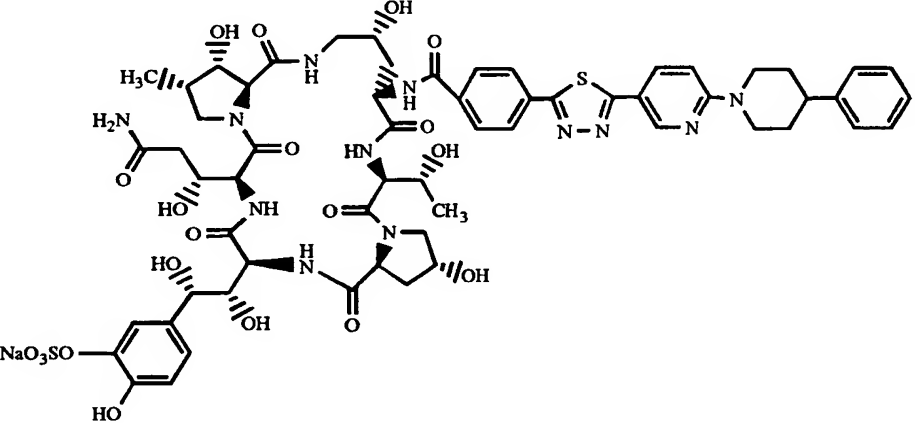
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
73	 <p>The structure is similar to the one above, but with a different side chain. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The side chain includes a triazole ring system and a long alkyl chain (O(CH<sub>2</sub>)<sub>4</sub>CH<sub>3</sub>).</p>

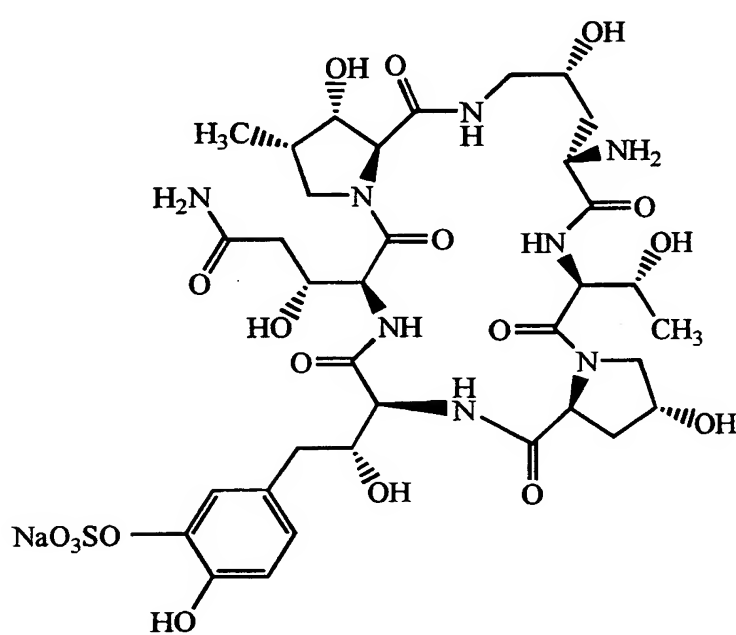
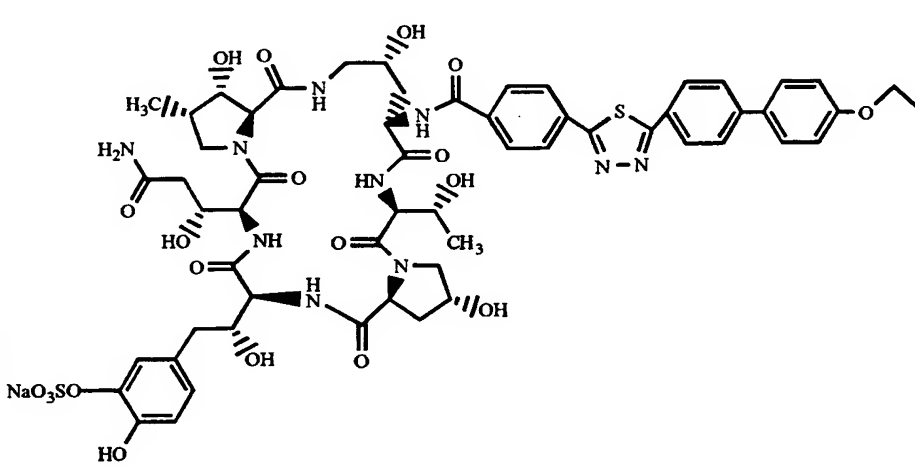
Example No.	Formula
74	 <p>The structure shows a complex molecule with multiple amide bonds, hydroxyl groups, and a sodium sulfonate group. It features a central chain with several side chains, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The molecule is highly branched and contains several functional groups.</p>
	 <p>This structure is similar to the one above, but it features a different side chain. It includes a sodium sulfonate group, a hydroxyl group, and a methyl group. The molecule is highly branched and contains several functional groups.</p>

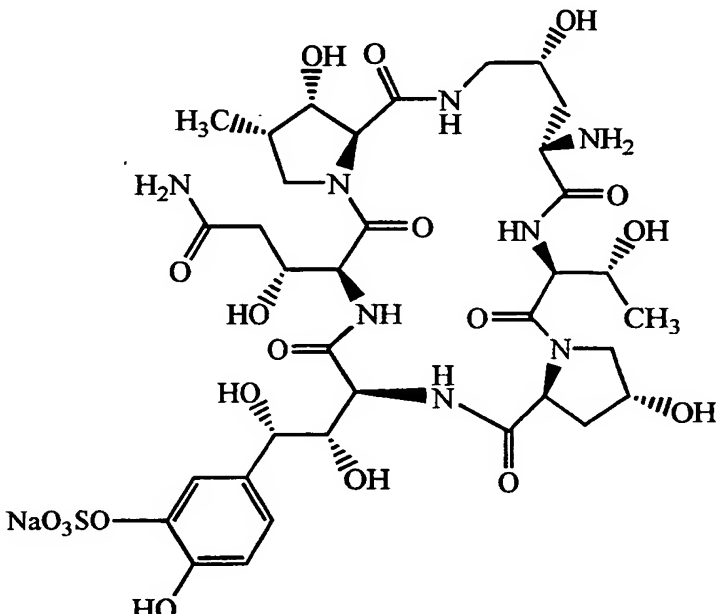
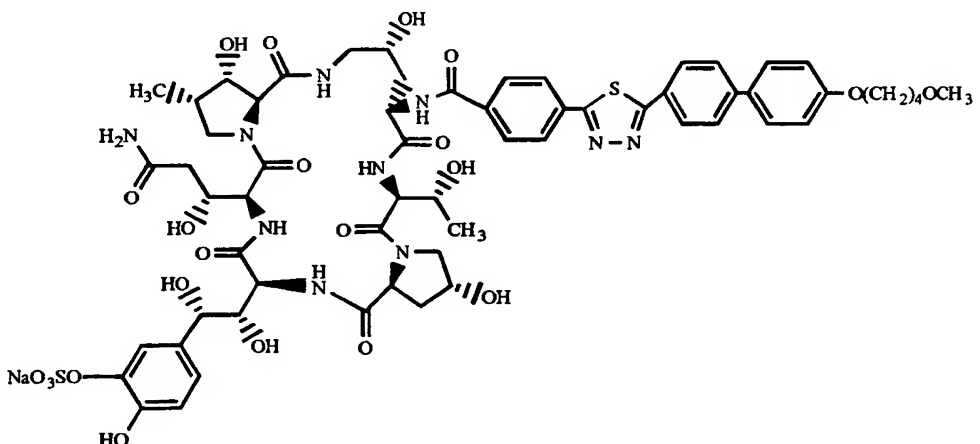
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
75	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>

Example No.	Formula
	
76	

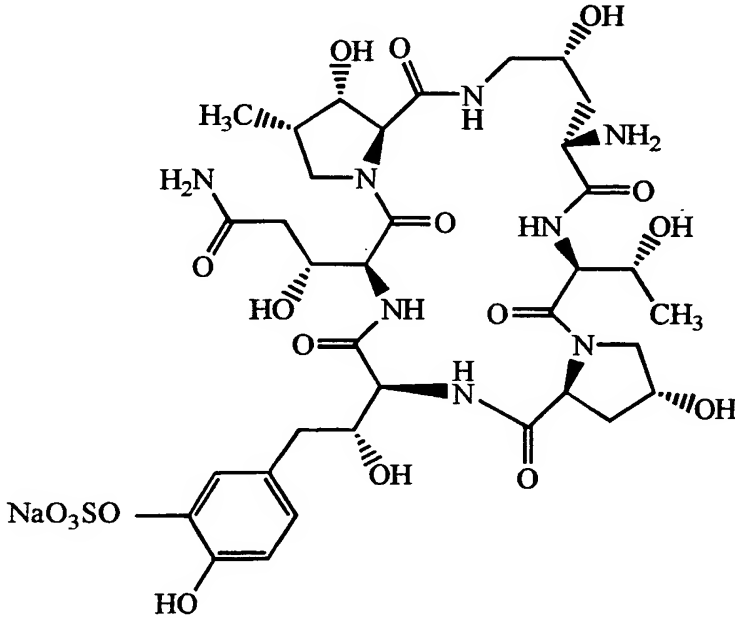
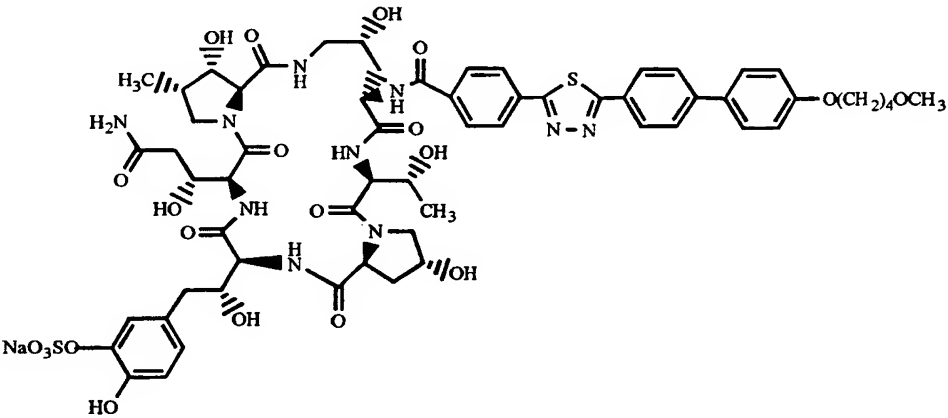
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group. It features a central chain with various side groups including a methyl group, a hydroxyl group, and a sulfonate group.</p>
77	 <p>This structure is similar to the one above but features a different side chain, including a sulfonamide group and a phenyl ring with a sodium sulfonate group.</p>

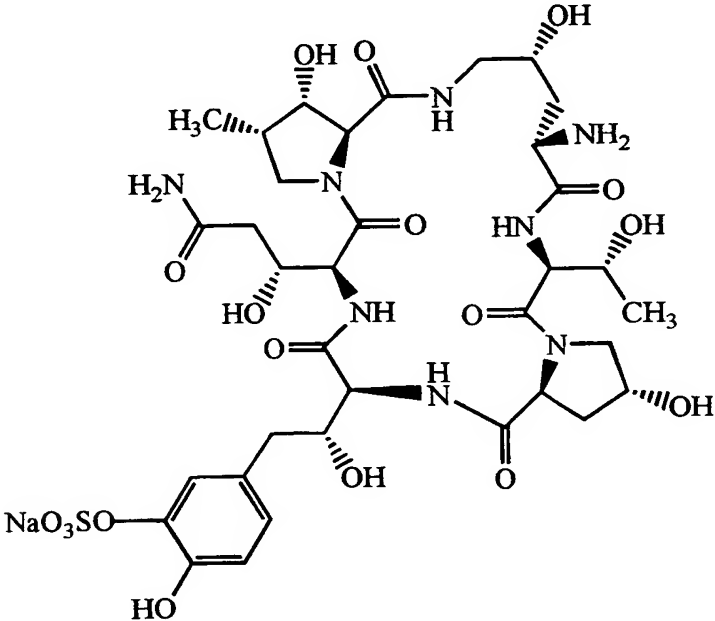
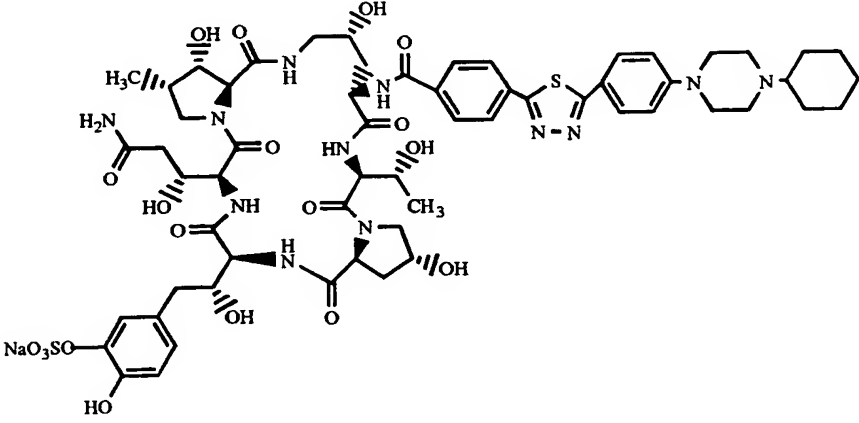
Example No.	Formula
78	
	

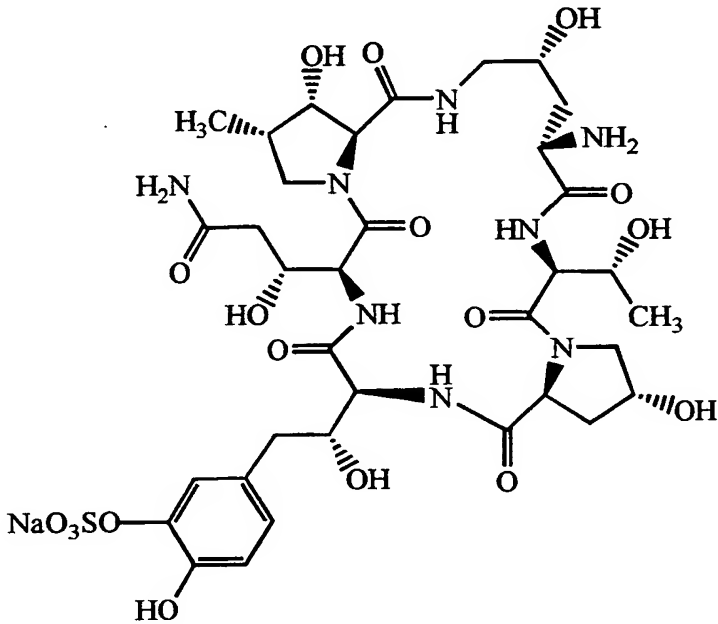
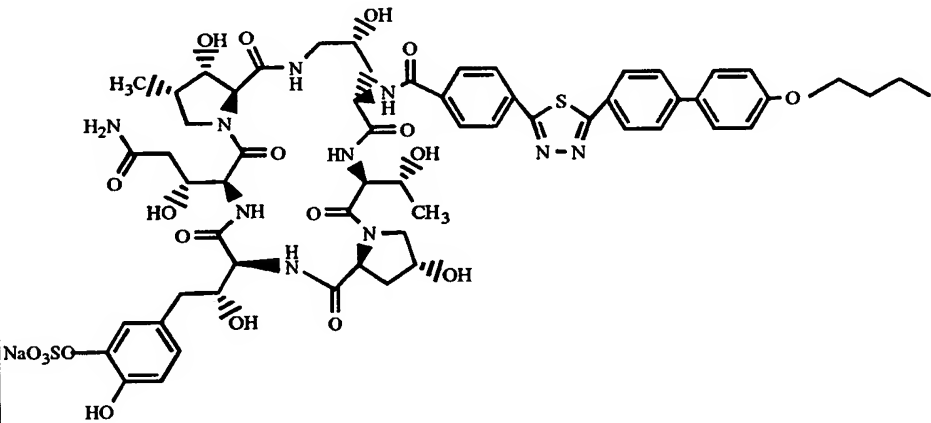
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple chiral centers, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group. It features a central amide linkage connecting two chiral fragments. One fragment includes a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-). The other fragment includes a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-). The molecule also contains several hydroxyl groups and amide bonds.</p>
79	 <p>This structure is similar to the one above but features a different side chain. It includes a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-). The molecule also contains several hydroxyl groups and amide bonds. The side chain is more complex, featuring a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-).</p>

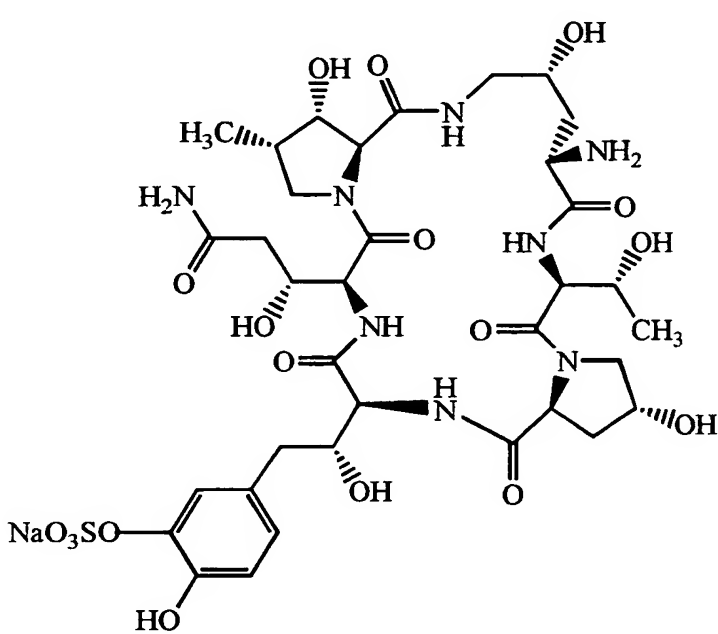
Example No.	Formula
	
80	

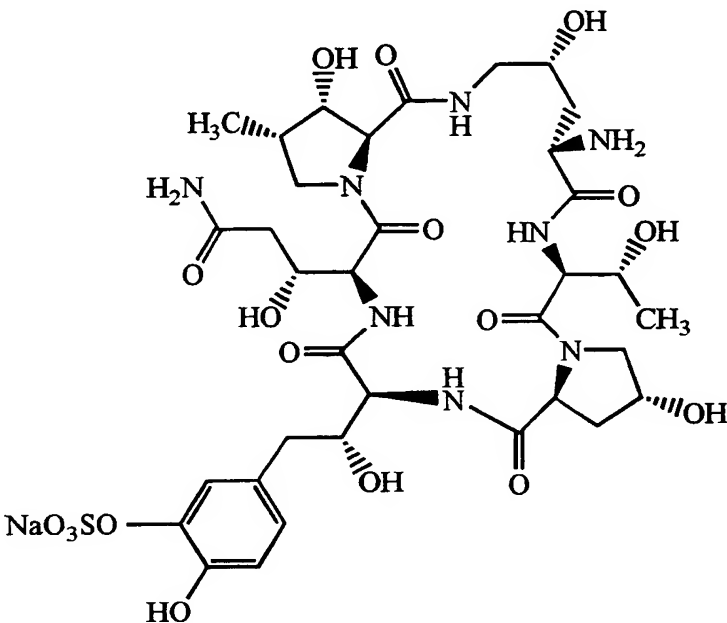
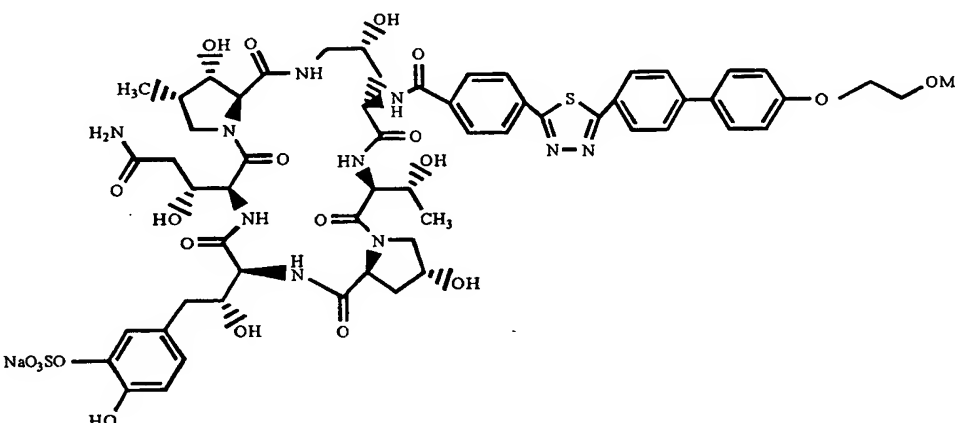


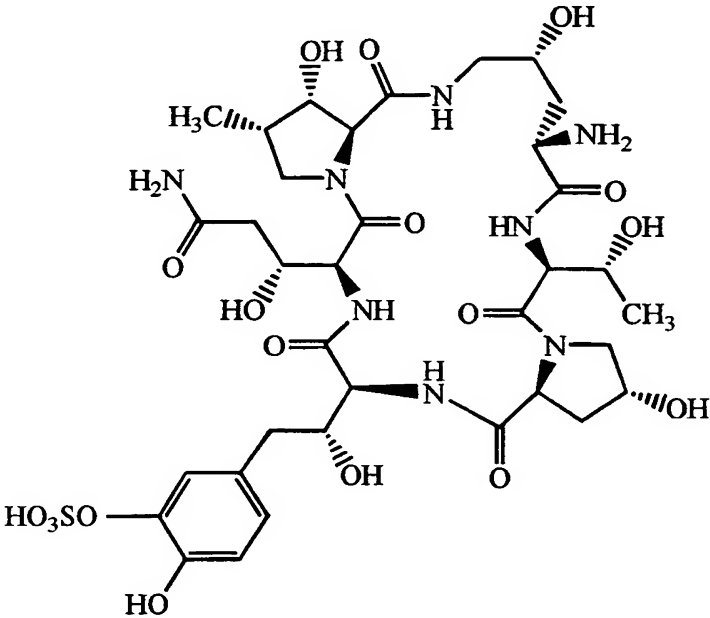
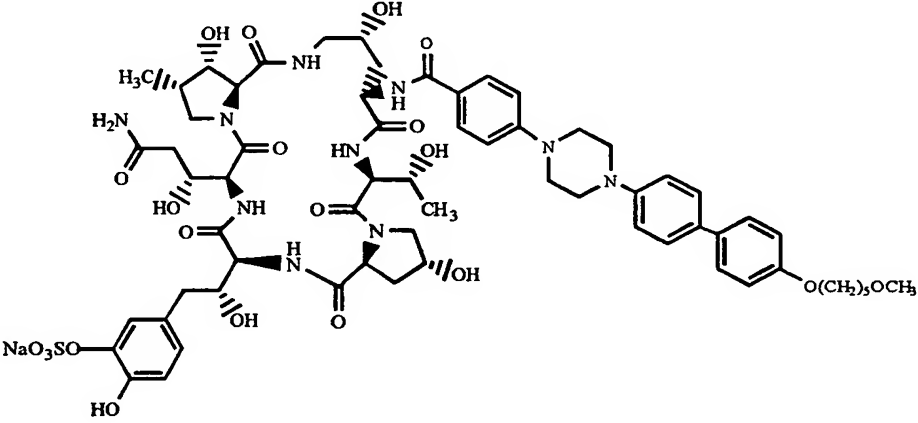
Example No.	Formula
	
81	

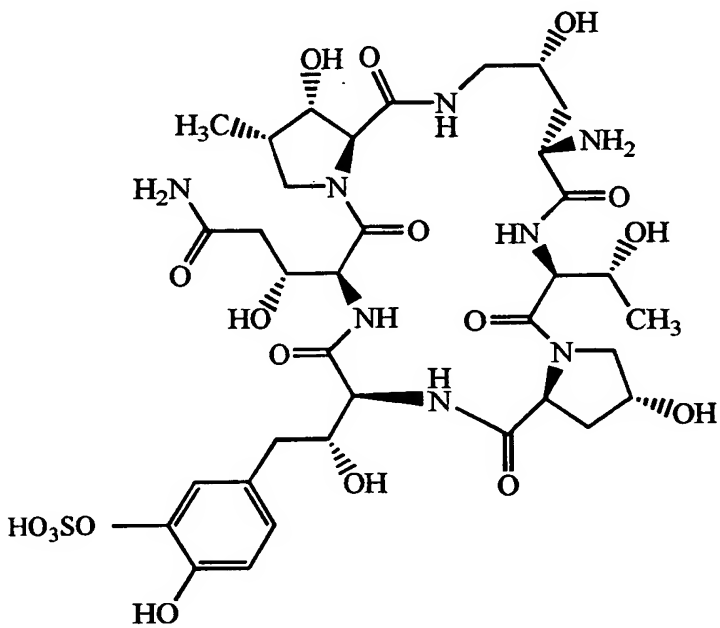
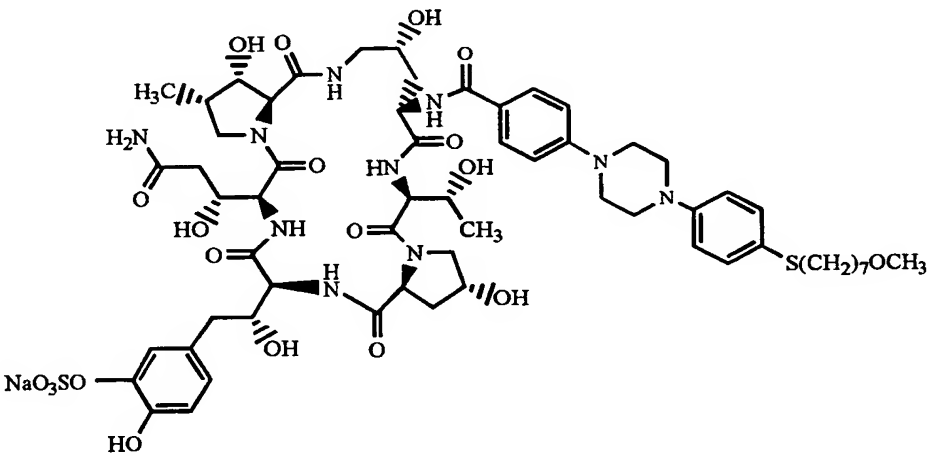
Example No.	Formula
	
82	

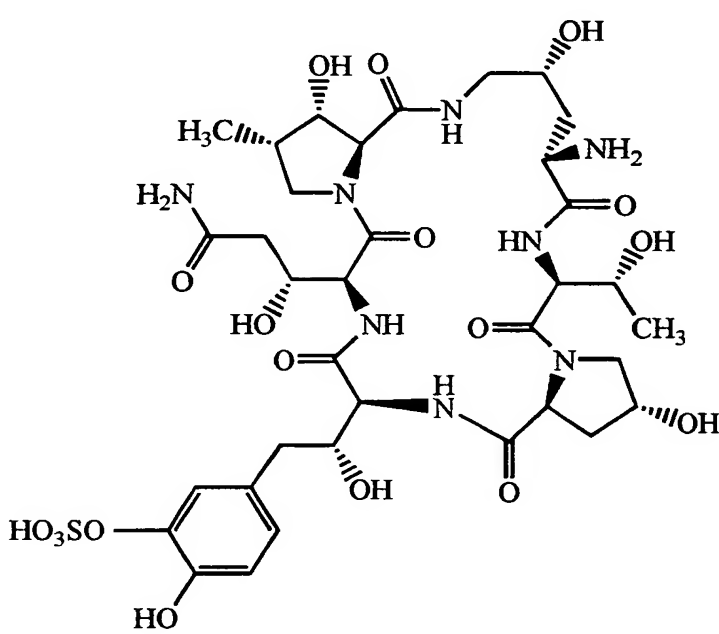
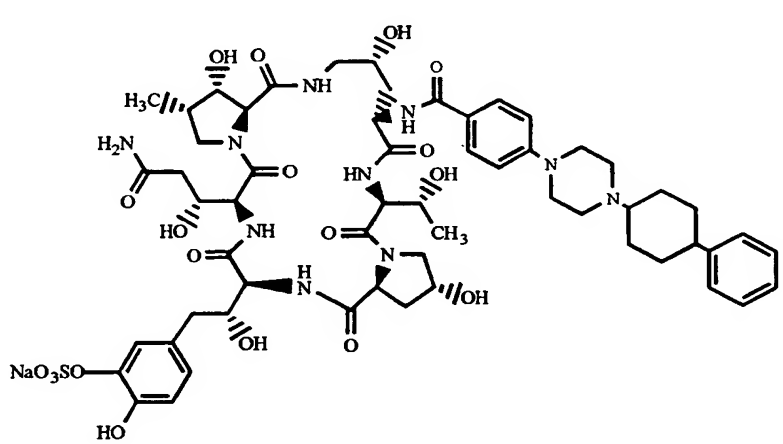
Example No.	Formula
	
83	

Example No.	Formula
84	 <p>The chemical structure shows a complex molecule with multiple stereocenters, amide bonds, and a sodium sulfonate group. It features a central core with various substituents, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The structure is highly detailed, showing the stereochemistry of the chiral centers and the connectivity of the atoms.</p>

Example No.	Formula
	
85	

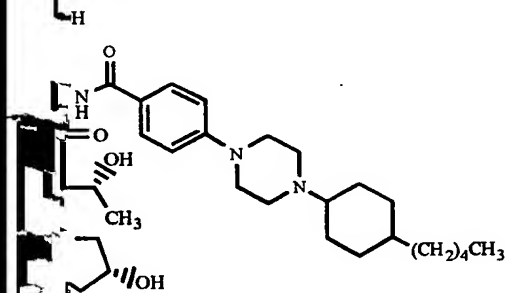
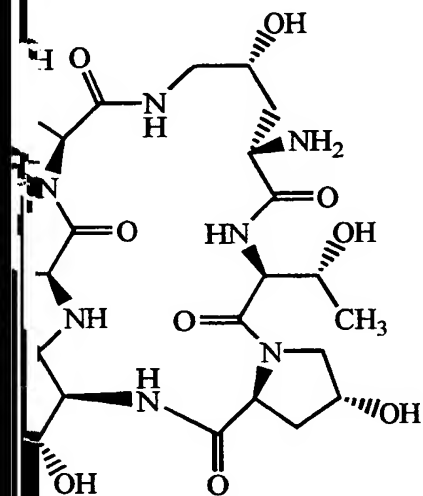
Example No.	Formula
	
86	

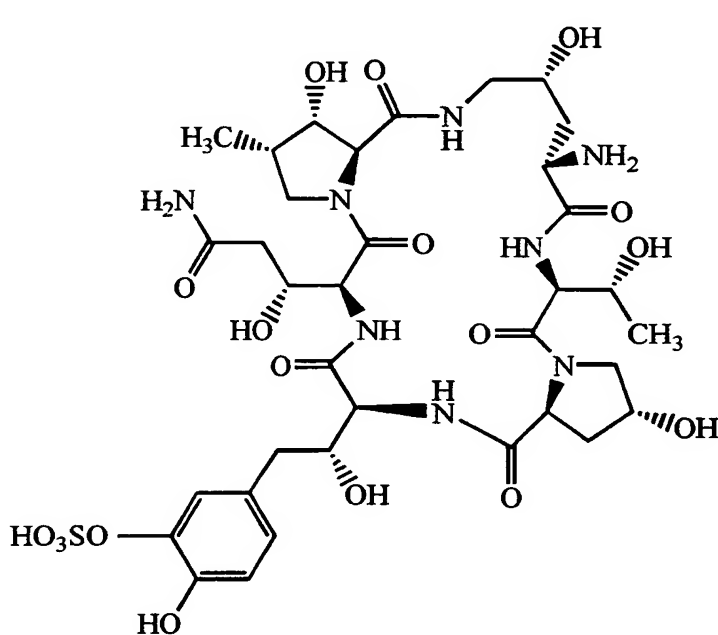
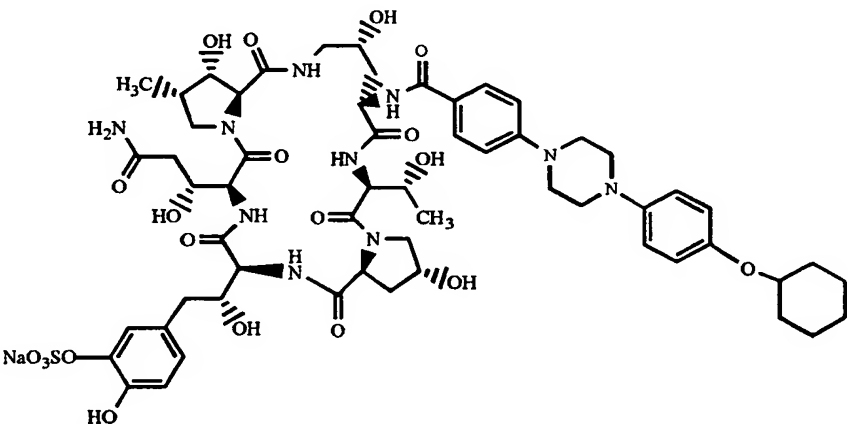
Example No.	Formula
	 <p>The structure shows a complex polycyclic molecule. It features a central core with several fused and linked rings, including a p-toluenesulfonate group (HO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly substituted with various functional groups and stereocenters.</p>
87	 <p>The structure shows a complex polycyclic molecule, similar to the one above but with different substituents. It features a sodium sulfonate group (NaO<sub>3</sub>SO-) and a long alkyl chain (S(CH<sub>2</sub>)<sub>7</sub>OCH<sub>3</sub>). The molecule is highly substituted with various functional groups and stereocenters.</p>

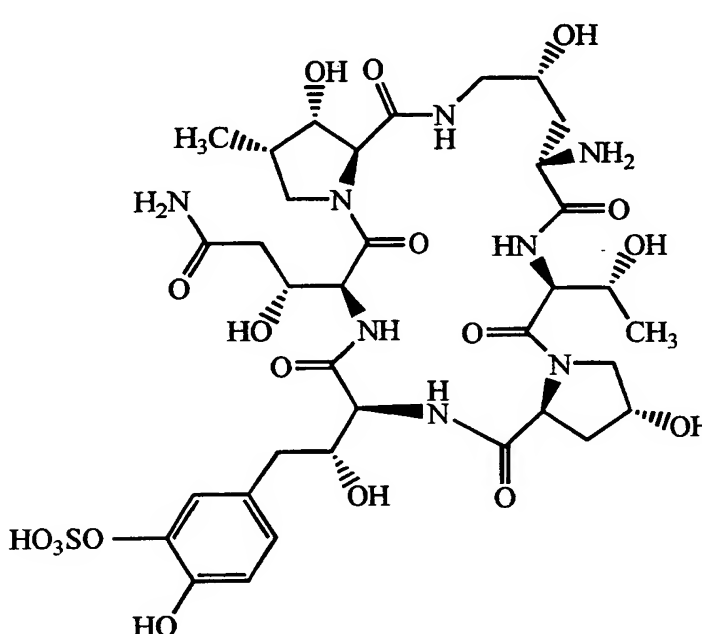
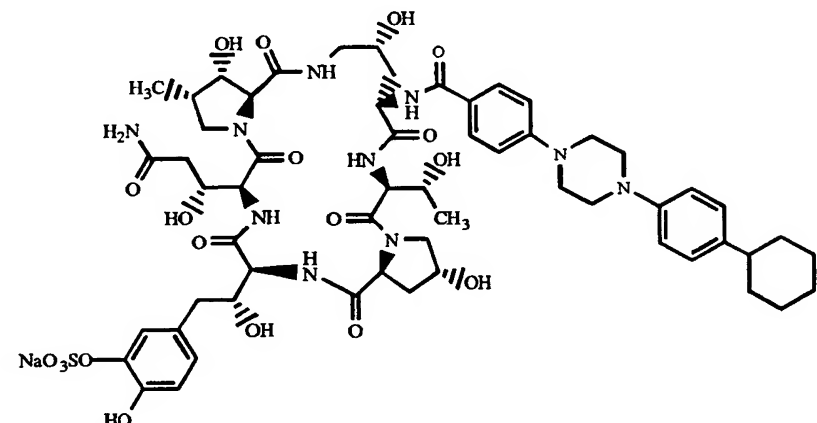
Example No.	Formula
	
88	

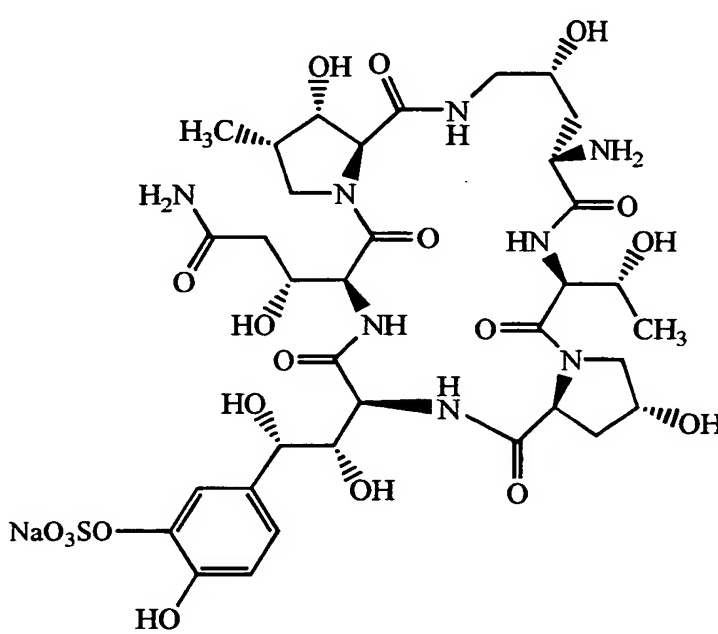
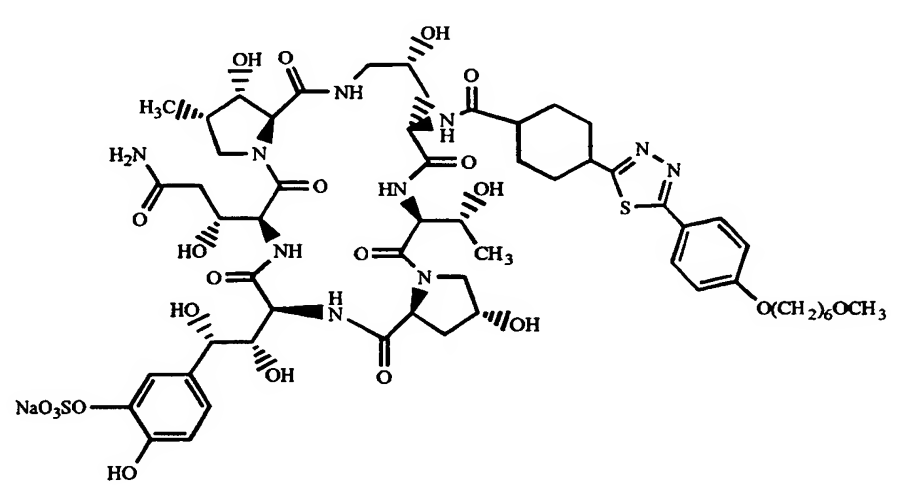


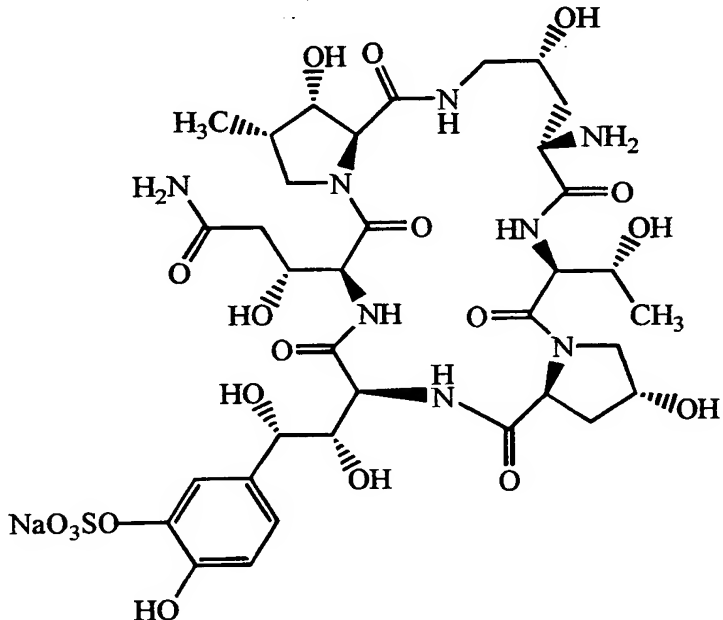
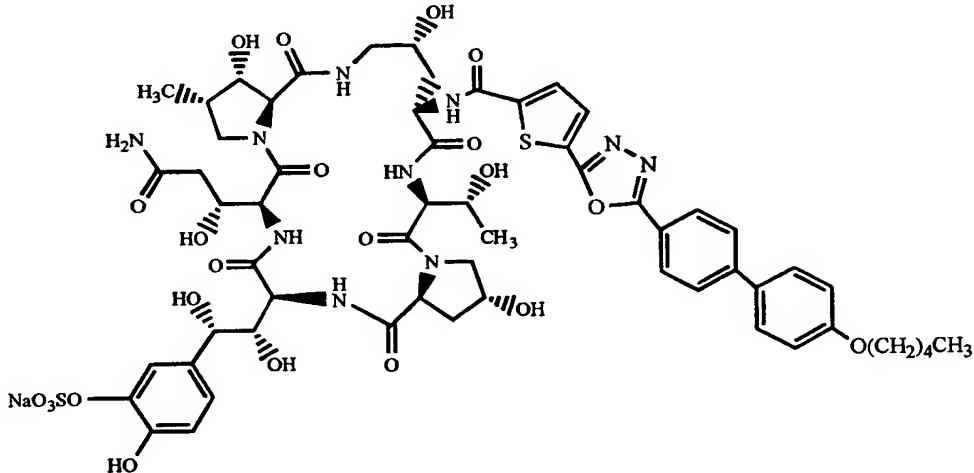
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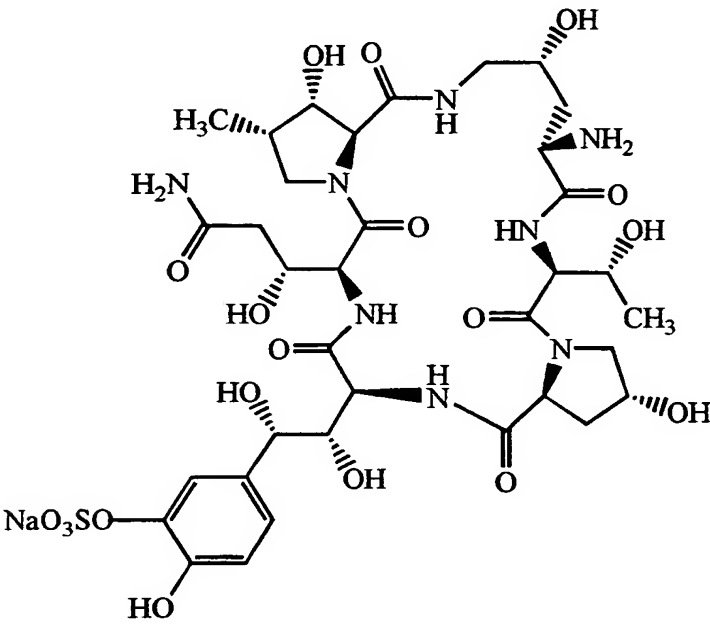
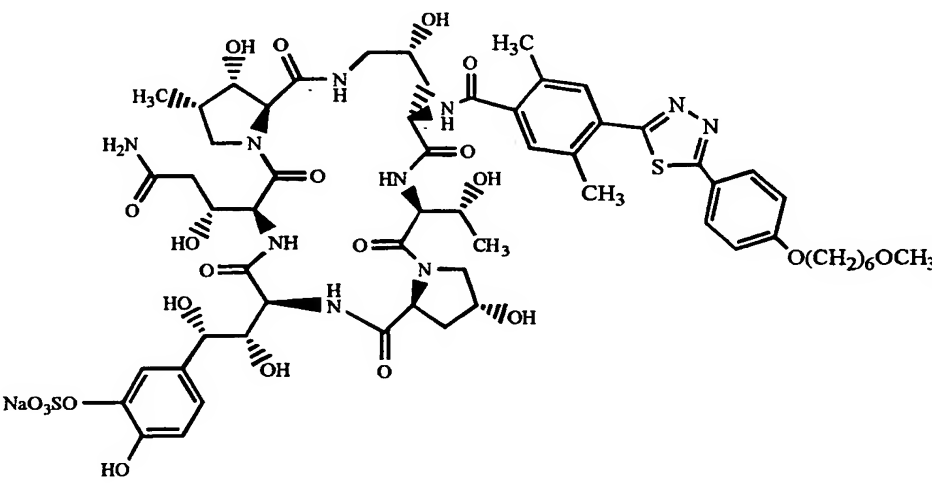


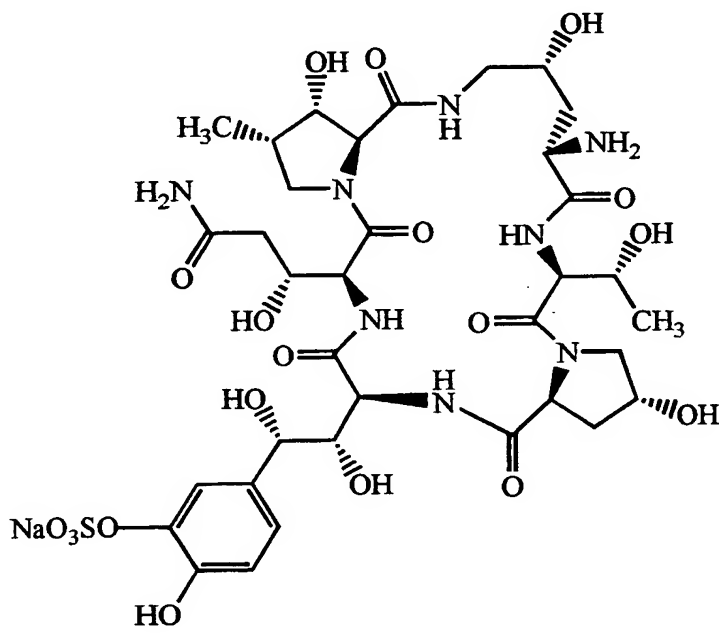
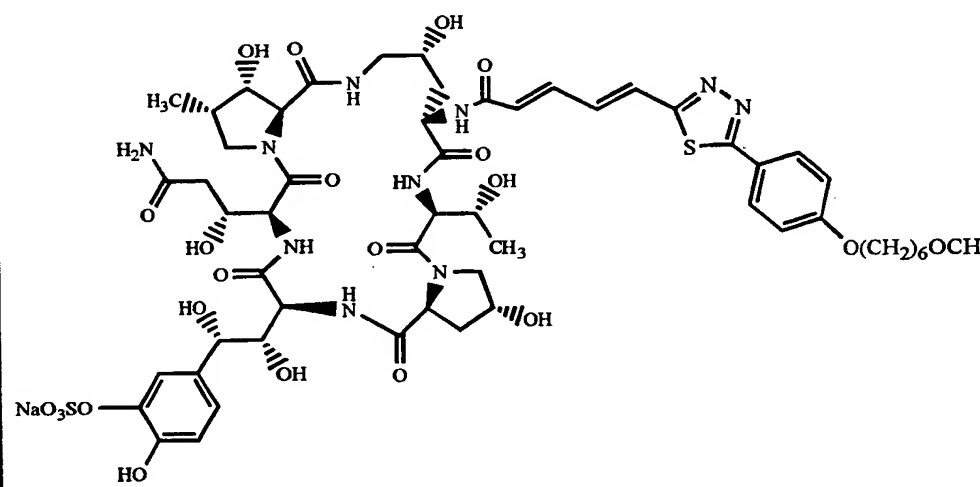
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a sulfonamide moiety (HO<sub>3</sub>SO-) and a hydroxyl group (HO-) on a benzene ring. The molecule is highly branched with various functional groups including amide, ester, and hydroxyl groups.</p>
90	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a sulfonamide moiety (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-) on a benzene ring. The molecule is highly branched with various functional groups including amide, ester, and hydroxyl groups.</p>

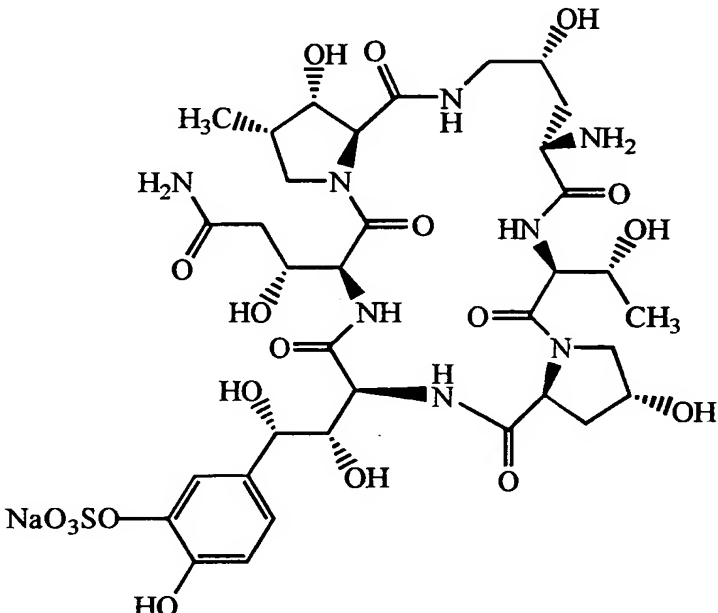
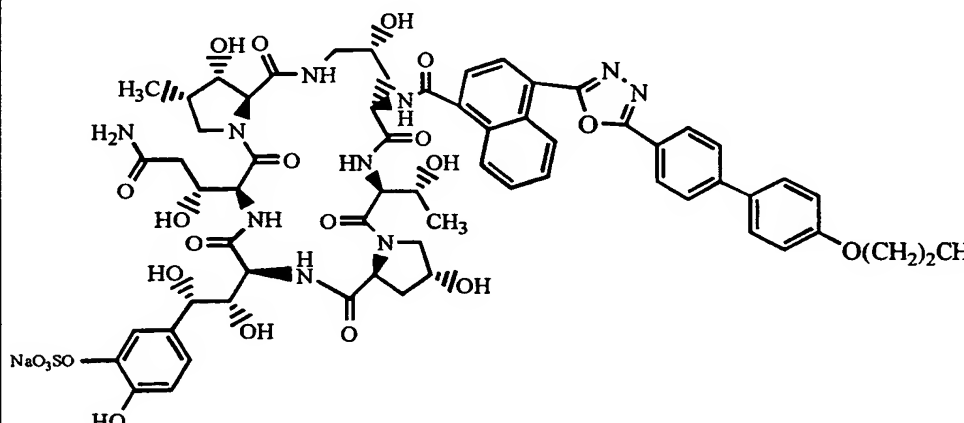
Example No.	Formula
	
91	

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central chain with several side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
92	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central chain with several side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds. It also includes a thiazine ring system and a hexamethylene chain.</p>

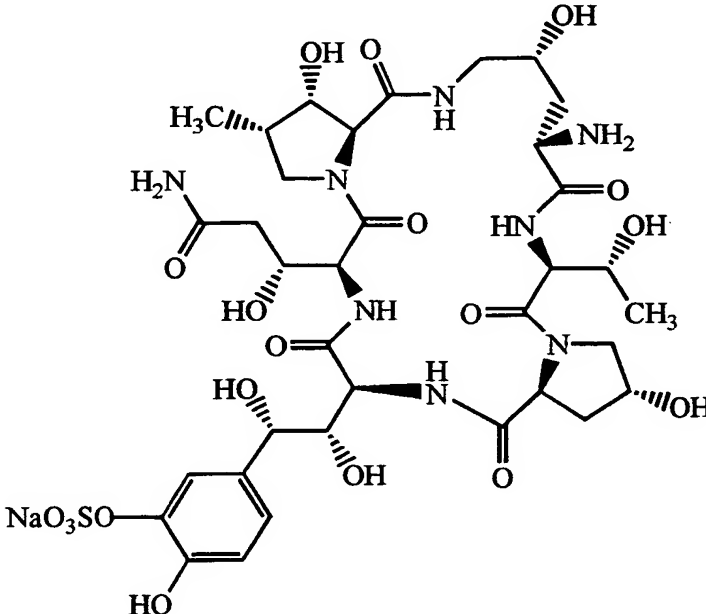
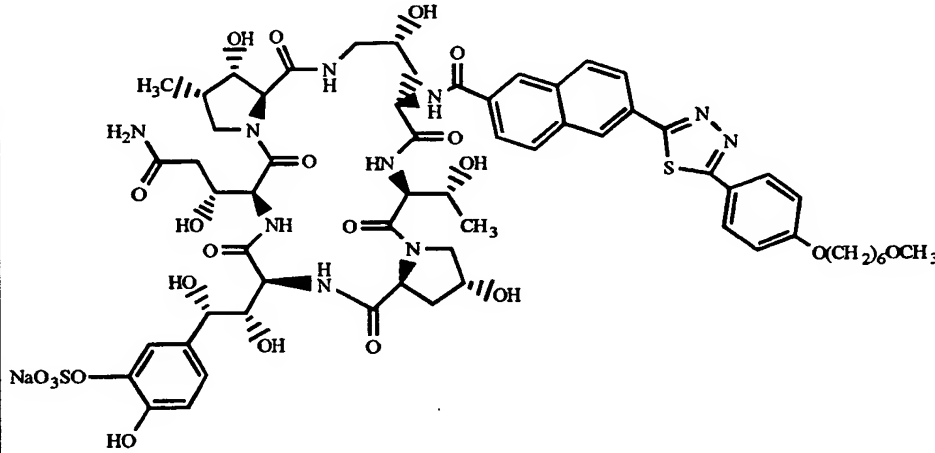
Example No.	Formula
	
93	

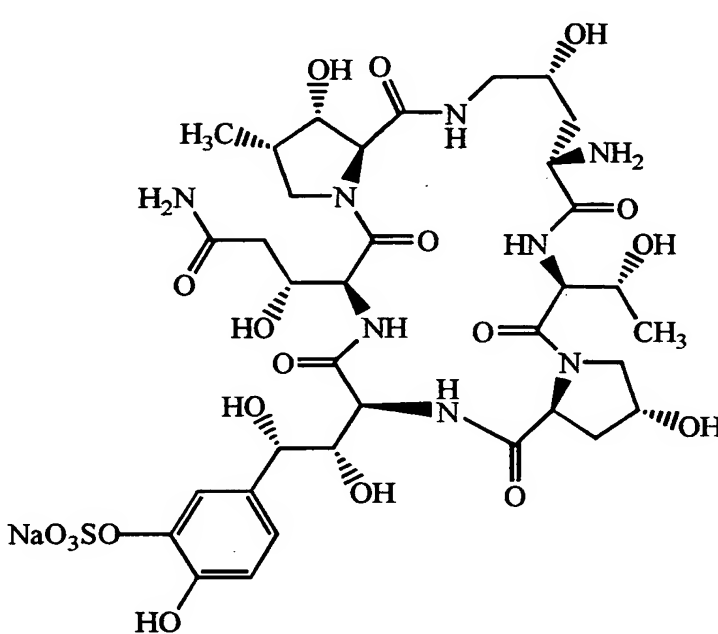
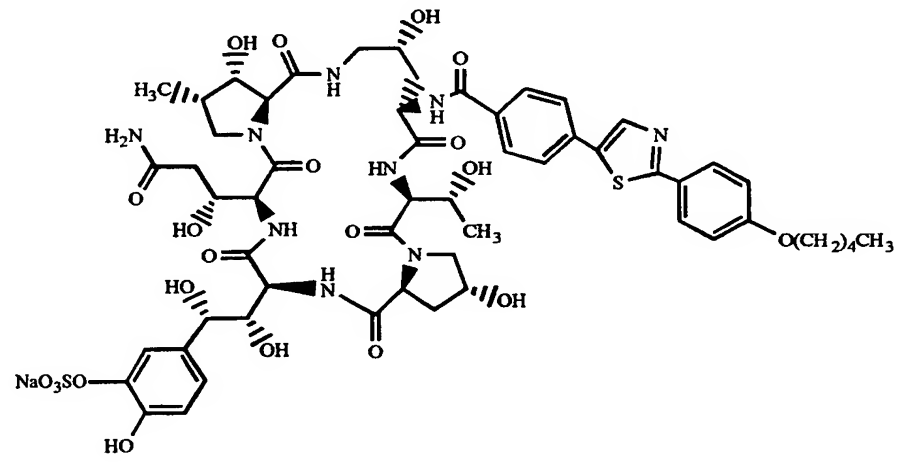
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group. The molecule is composed of several interconnected rings and functional groups, including a 4-hydroxyphenyl group with a sodium sulfonate group, a 4-methylphenyl group, and a 4-methylphenyl group with a sodium sulfonate group.</p>
94	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group. The molecule is composed of several interconnected rings and functional groups, including a 4-hydroxyphenyl group with a sodium sulfonate group, a 4-methylphenyl group, and a 4-methylphenyl group with a sodium sulfonate group.</p>

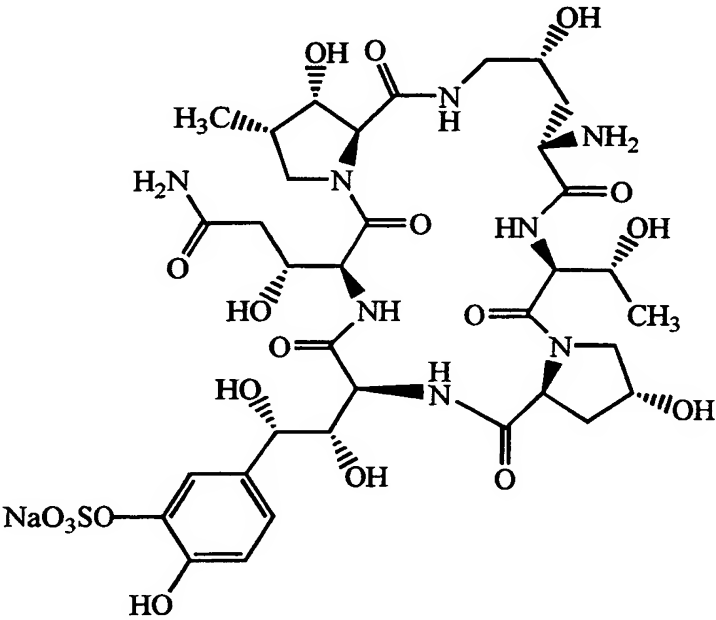
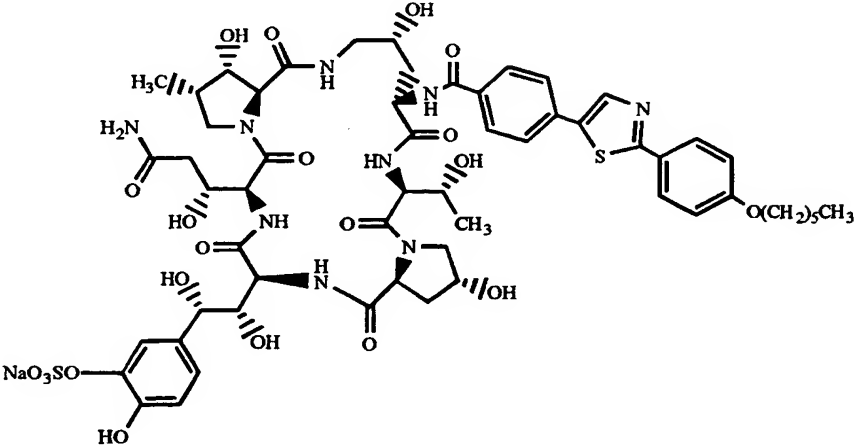
Example No.	Formula
	
95	

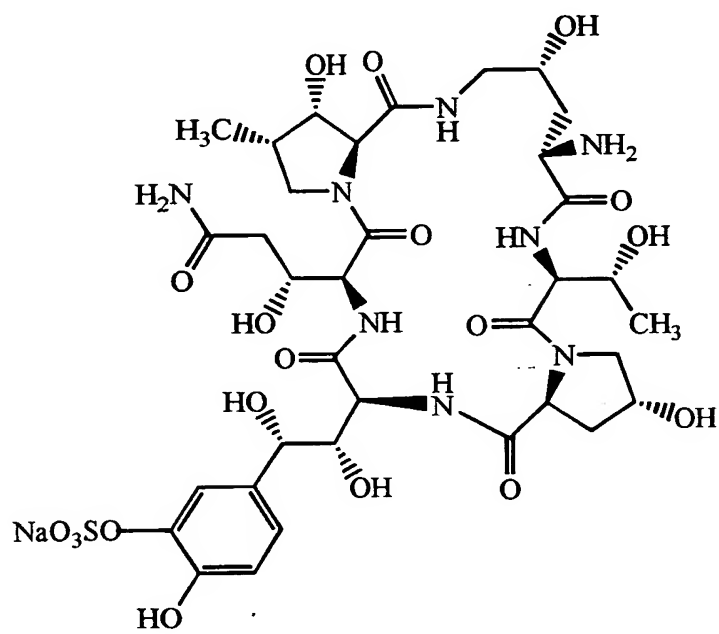
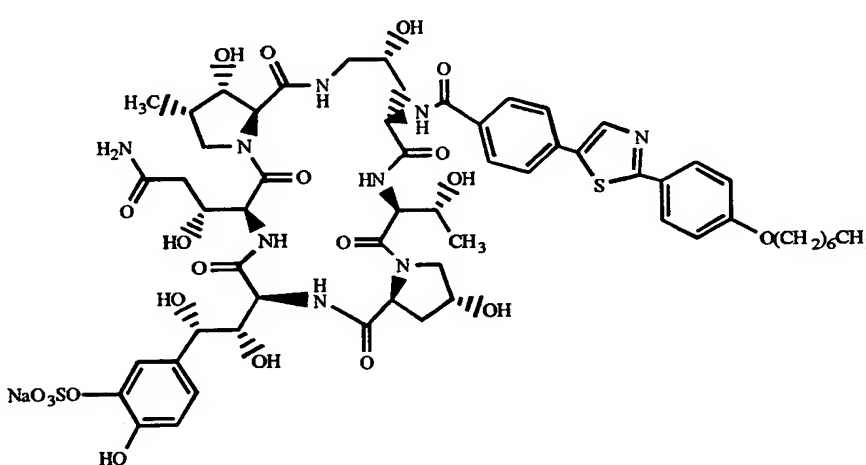
Example No.	Formula
	
96	

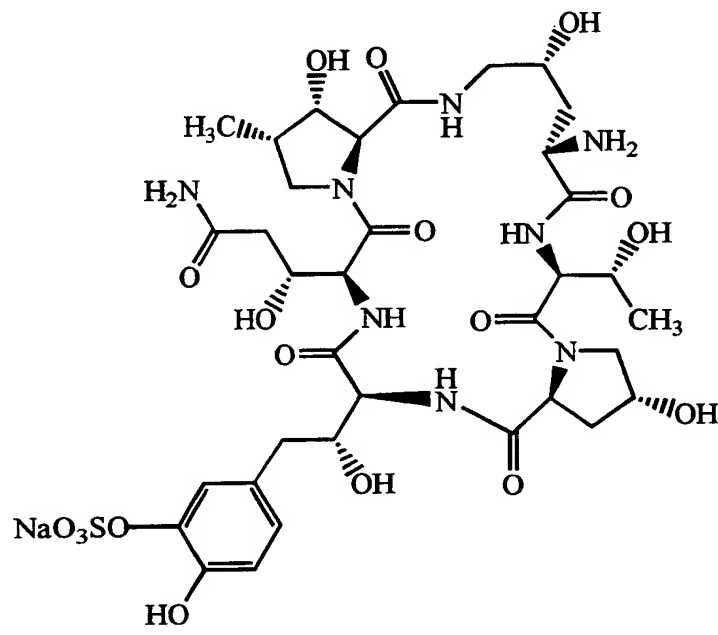
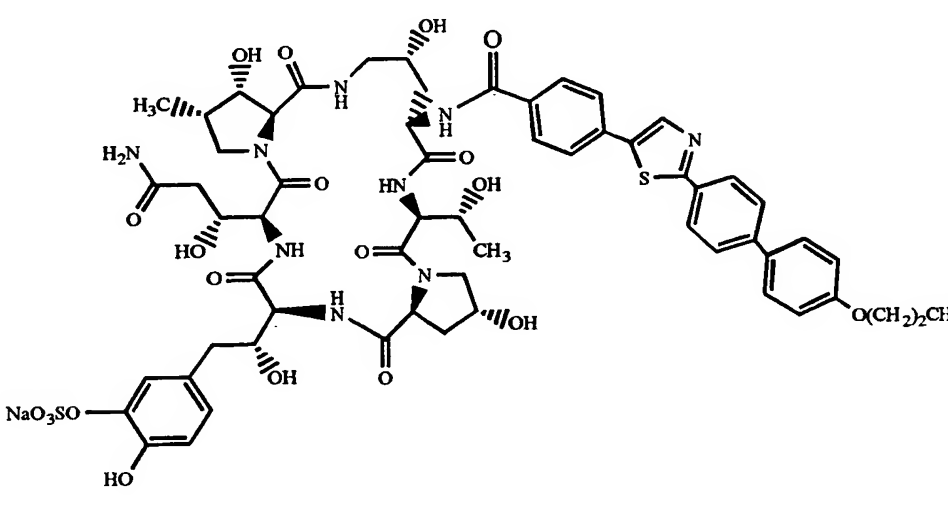


Example No.	Formula
	
97	

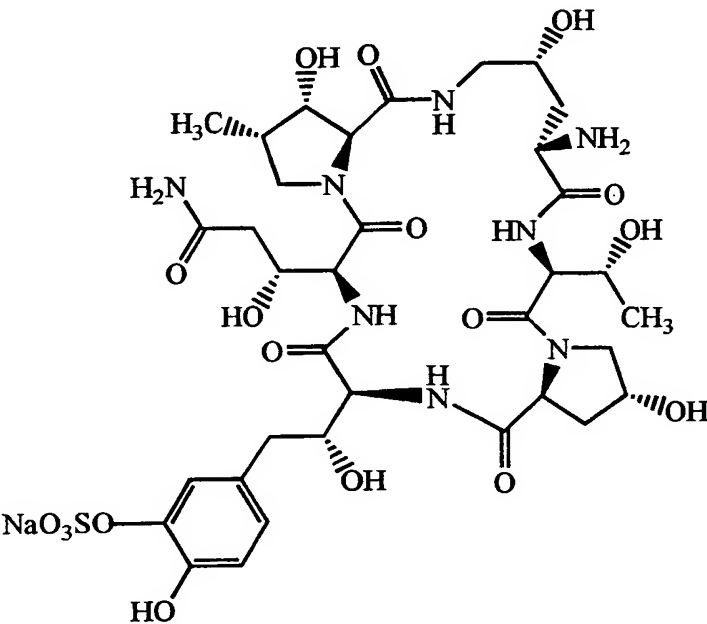
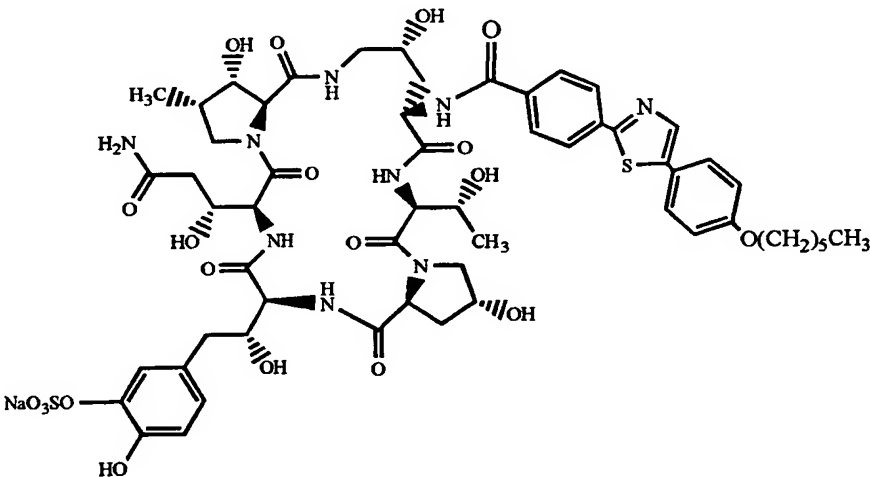
Example No.	Formula
	
98	

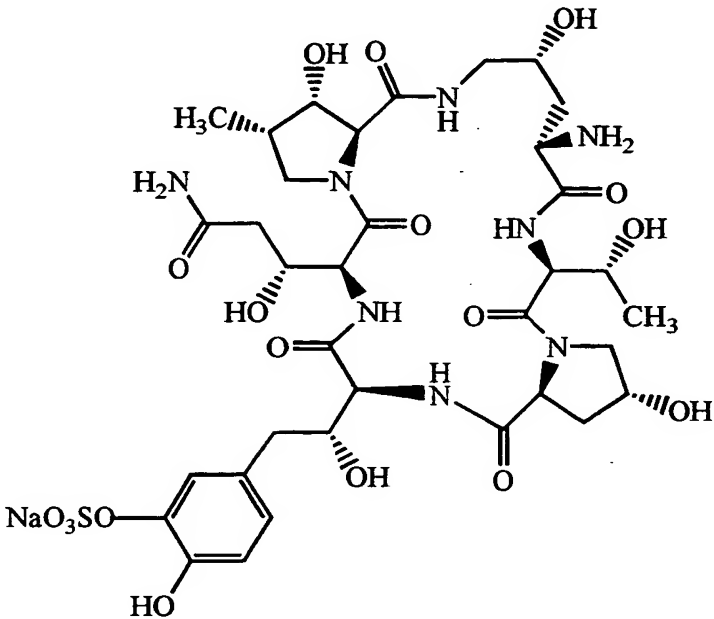
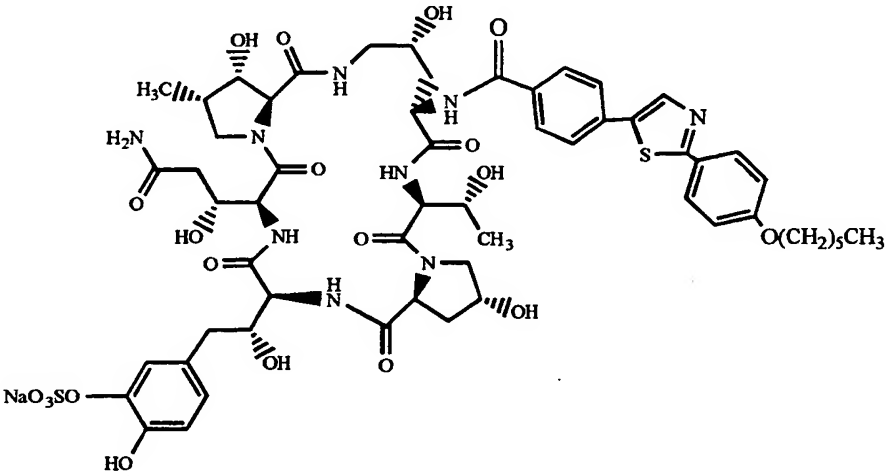
Example No.	Formula
	 <p>The structure is a complex molecule featuring several stereocenters indicated by wedges and dashes. It includes amide bonds, hydroxyl groups, a methyl group, and a 3-hydroxy-4-sulfonatophenyl group (NaO<sub>3</sub>SO-). The molecule is highly branched and contains multiple nitrogen and oxygen atoms.</p>
99	 <p>This structure is similar to the one in the first row, but it features a different side chain. It includes a 3-hydroxy-4-sulfonatophenyl group (NaO<sub>3</sub>SO-), a methyl group, and a side chain that includes a thiazole ring and a 4-ethoxyphenyl group (O(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>).</p>

Example No.	Formula
100	 <p>The structure shows a complex molecule with multiple chiral centers, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group. It features a central amide linkage connecting two chiral fragments. One fragment includes a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-). The other fragment includes a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-).</p>
	 <p>The structure shows a complex molecule with multiple chiral centers, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group. It features a central amide linkage connecting two chiral fragments. One fragment includes a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-). The other fragment includes a 4-hydroxyphenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO-).</p>

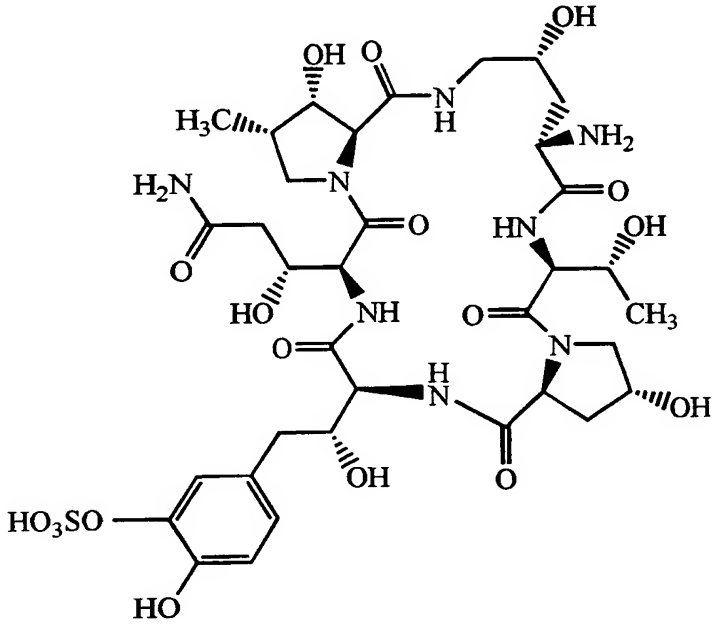
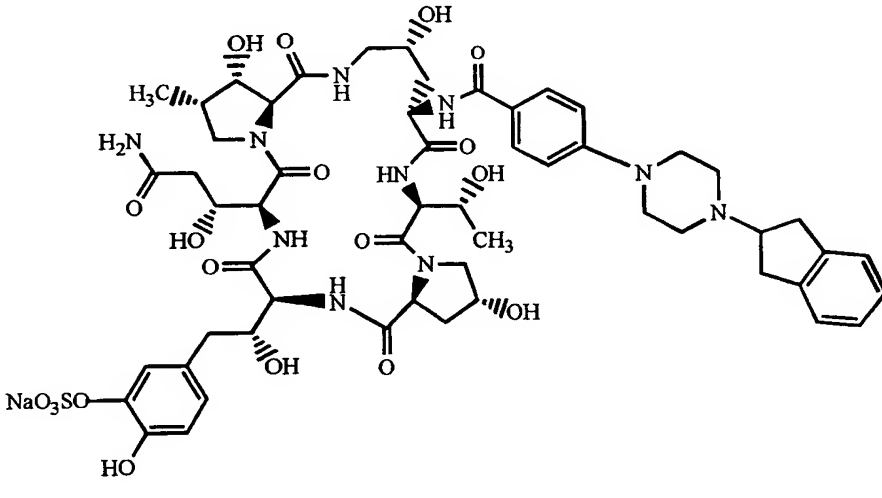
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). Stereochemistry is indicated with wedges and dashes.</p>
101	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). Stereochemistry is indicated with wedges and dashes.</p>

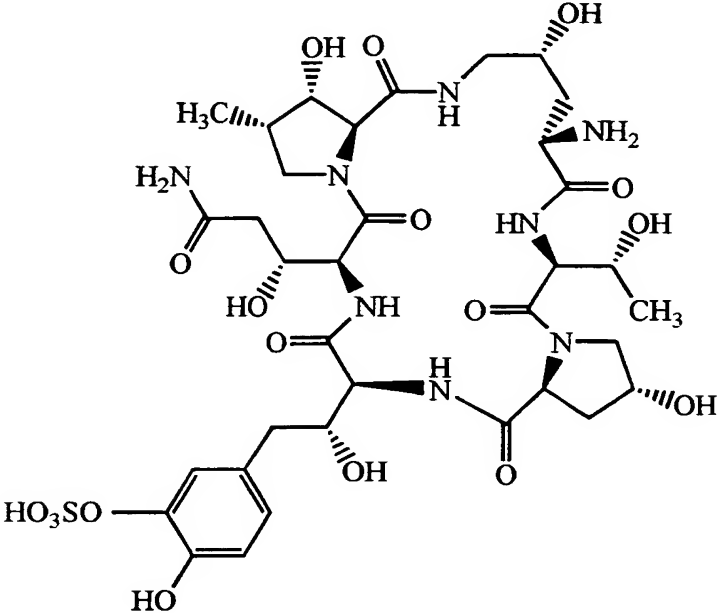
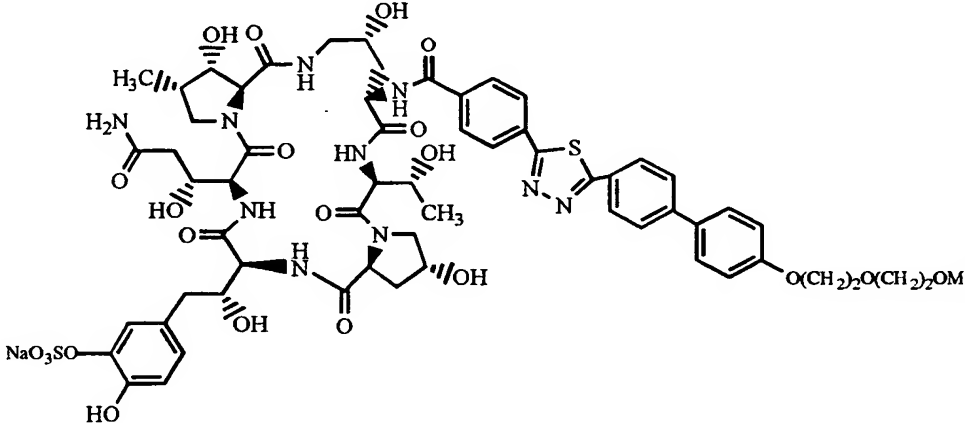
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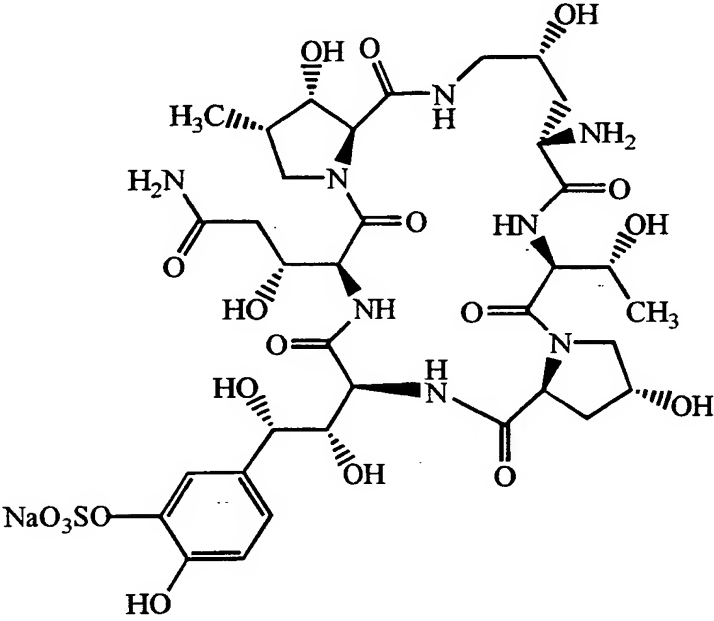
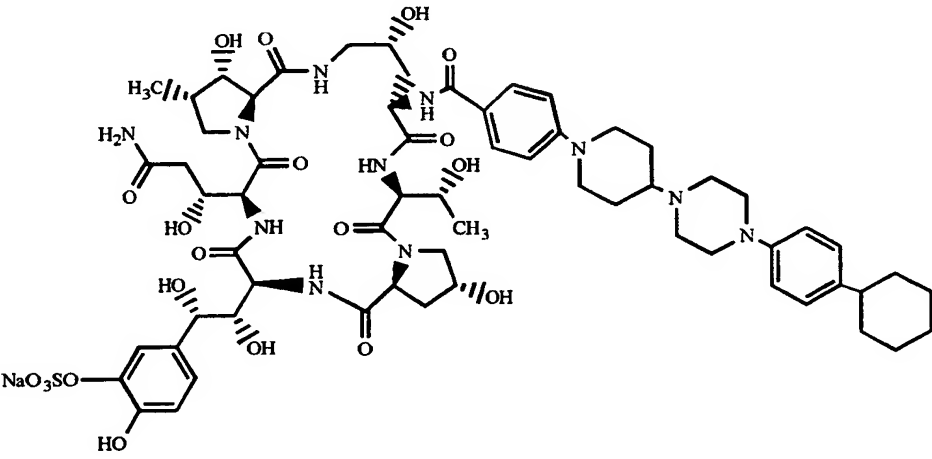
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide and ester linkages. It features a central core with various side chains, including a hydroxyl group, a methyl group, and a sodium sulfonate group (NaO<sub>3</sub>SO-). The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
103	 <p>This structure is similar to the one above, but it features a different side chain. It includes a hydroxyl group, a methyl group, and a sodium sulfonate group (NaO<sub>3</sub>SO-). The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds. The side chain on the right is more complex, featuring a thiazole ring and a long alkyl chain (O(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>).</p>

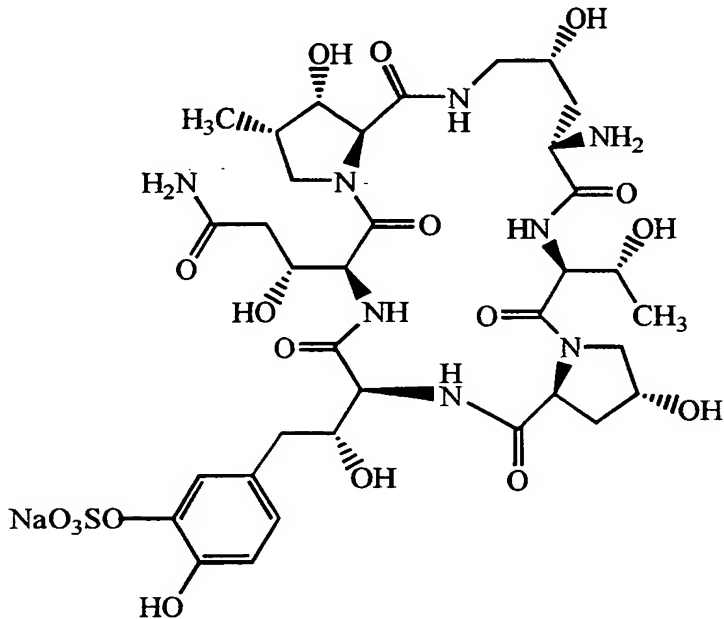
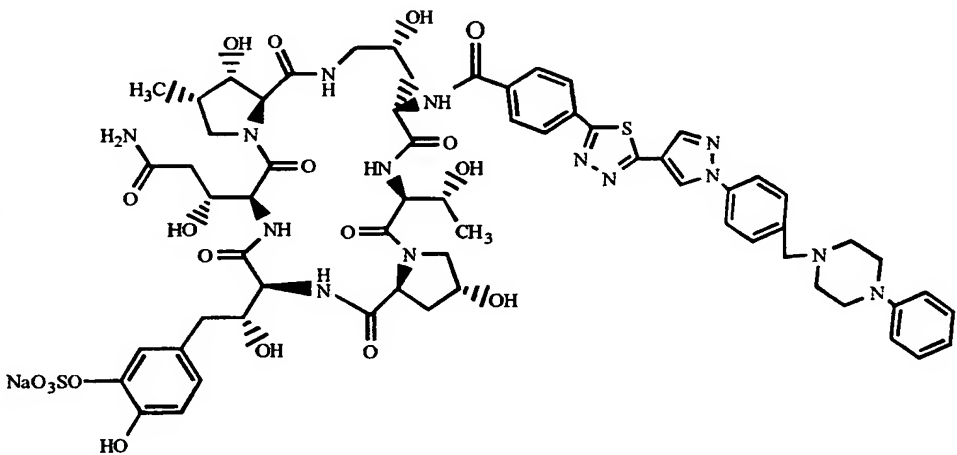
Example No.	Formula
	
104	

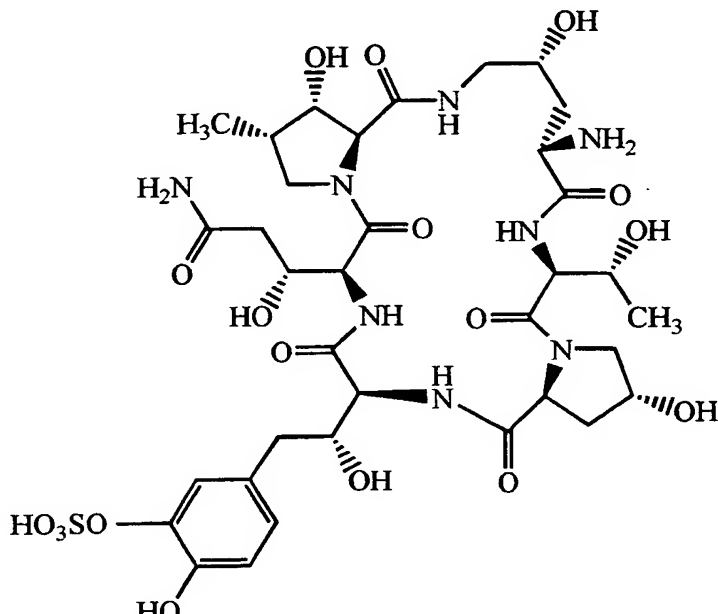
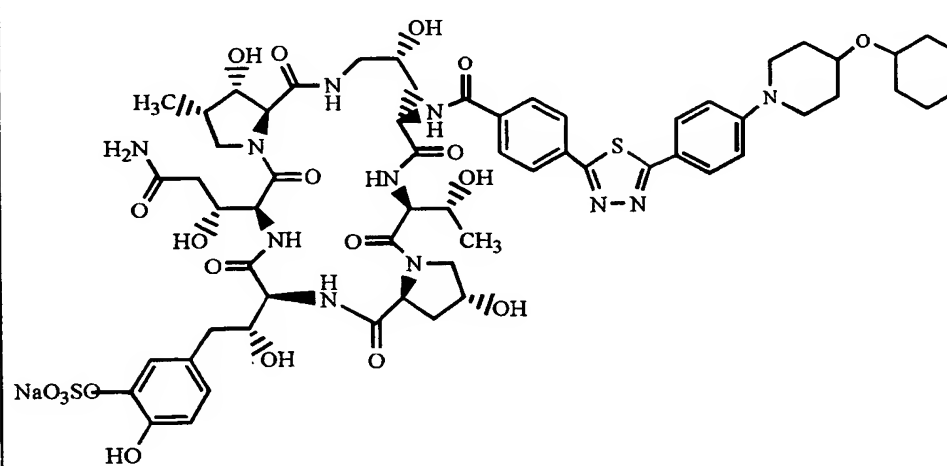


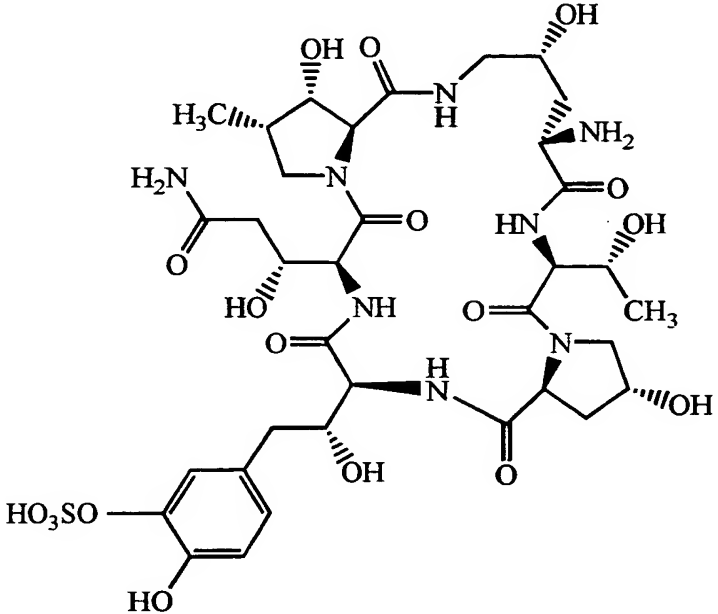
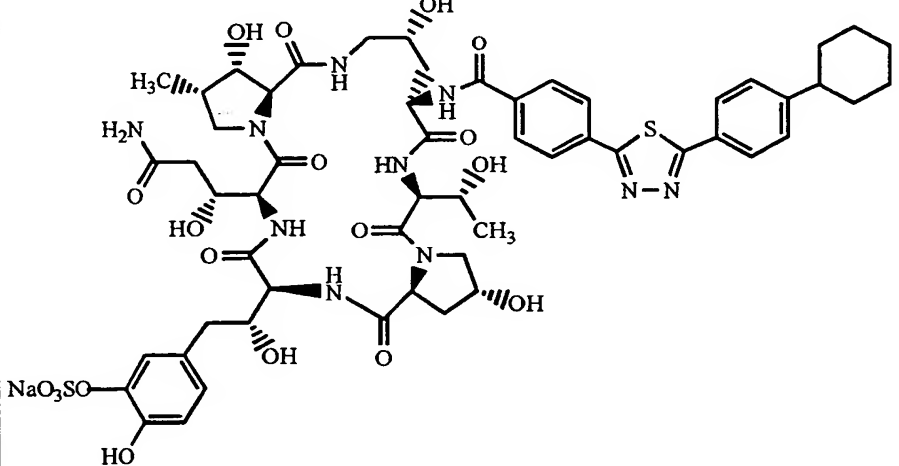
Example No.	Formula
	
105	

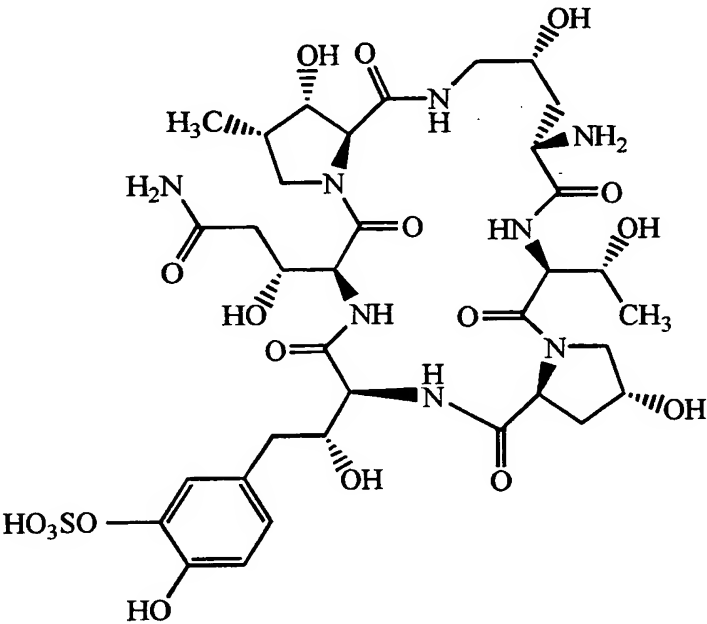
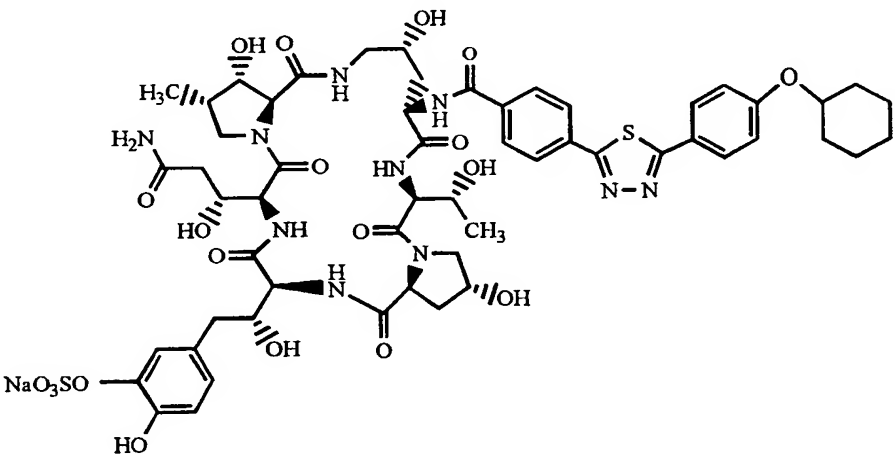
Example No.	Formula
	
106	

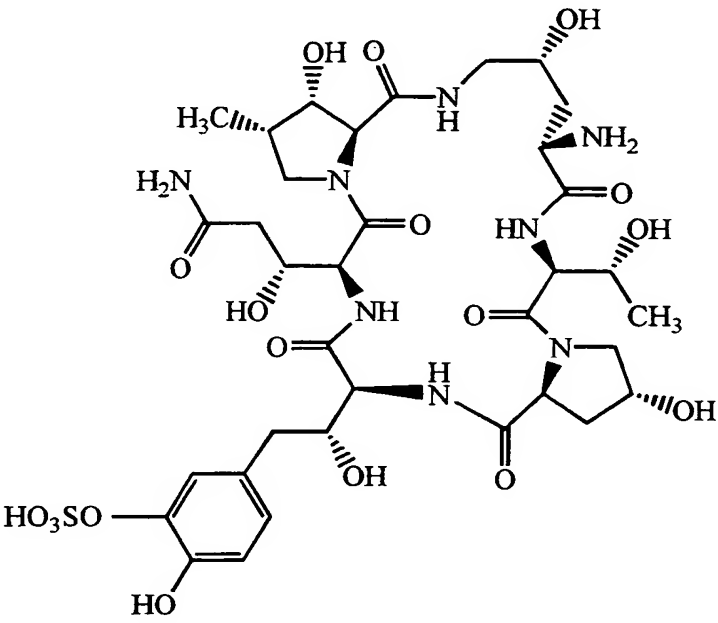
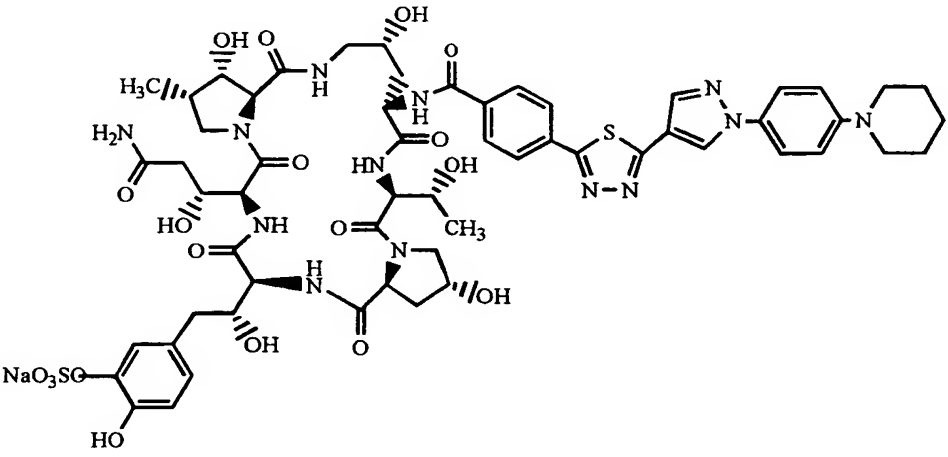
Example No.	Formula
	
107	

Example No.	Formula
	
108	

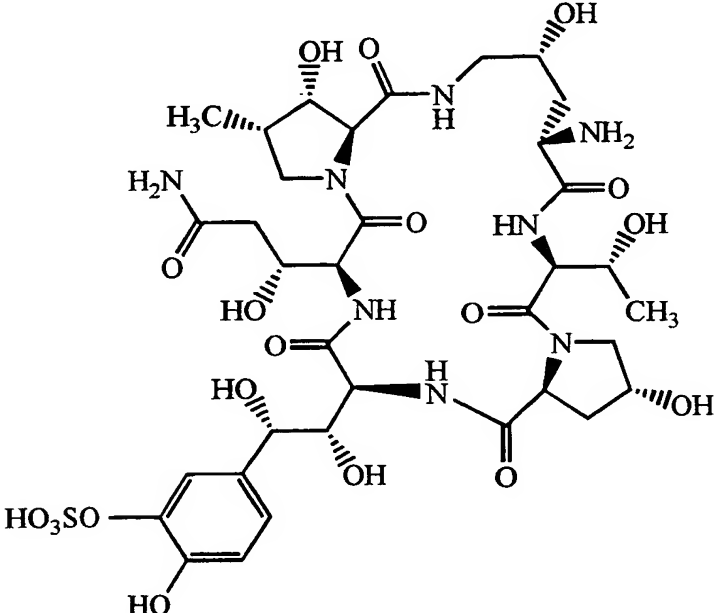
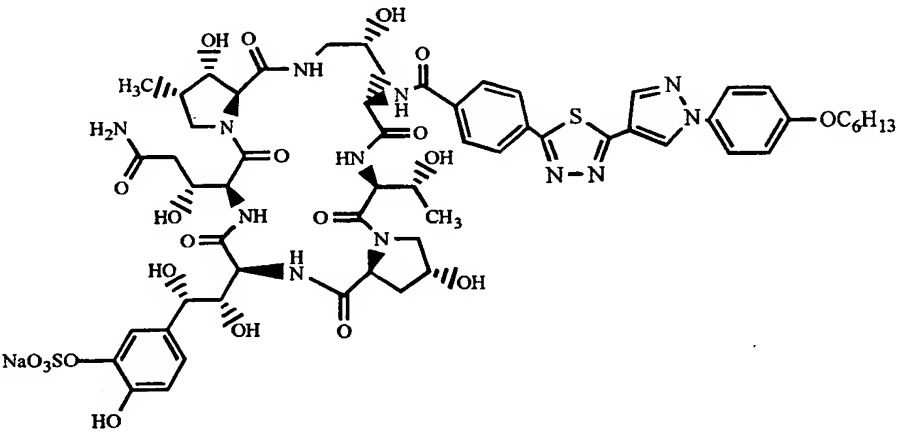
Example No.	Formula
	
109	

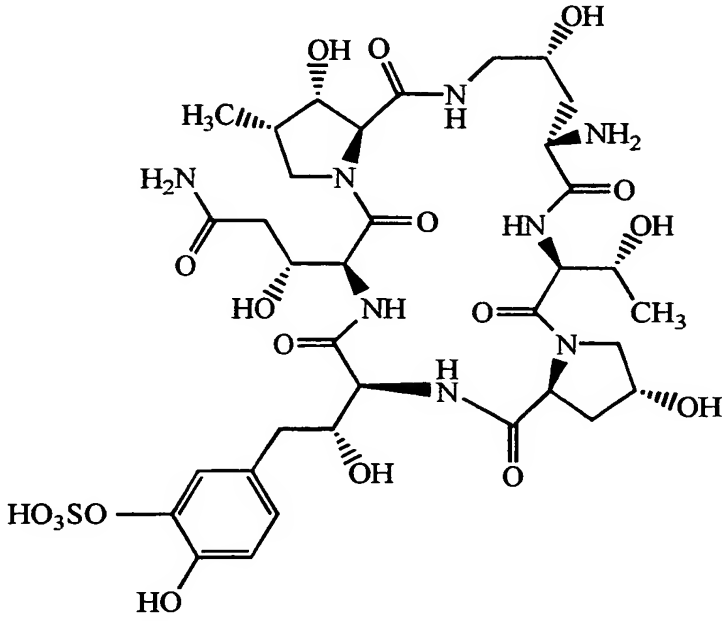
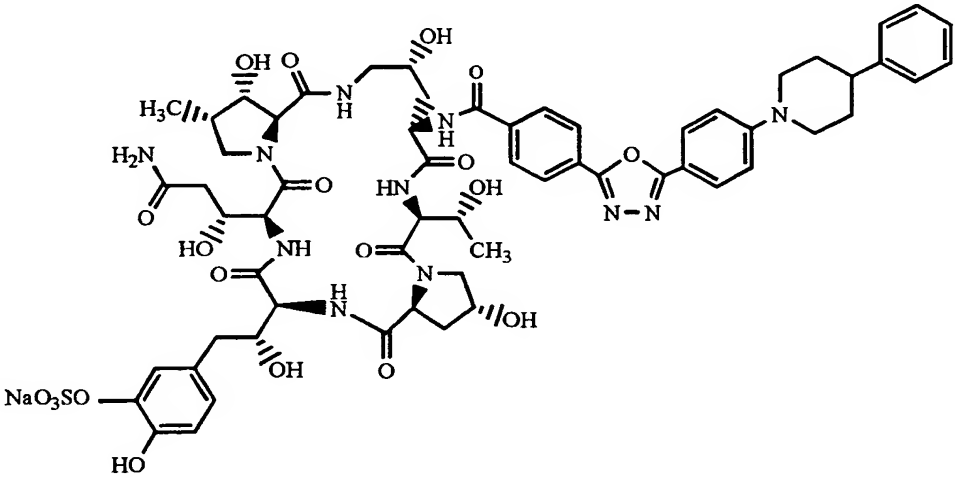
Example No.	Formula
110	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfonatephenyl group. It features a central chain with several amide linkages and hydroxyl groups. A 4-hydroxy-3-sulfonatephenyl group is attached to the chain. The molecule is highly branched and contains several chiral centers indicated by wedges and dashes.</p>
110	 <p>This structure is similar to the one above but features a different side chain. It includes a 4-hydroxy-3-sulfonatephenyl group (with NaO<sub>3</sub>SO) and a side chain containing a 1,3,4-oxadiazole ring and a cyclohexyl group. The molecule has multiple stereocenters and amide bonds, with chiral centers indicated by wedges and dashes.</p>

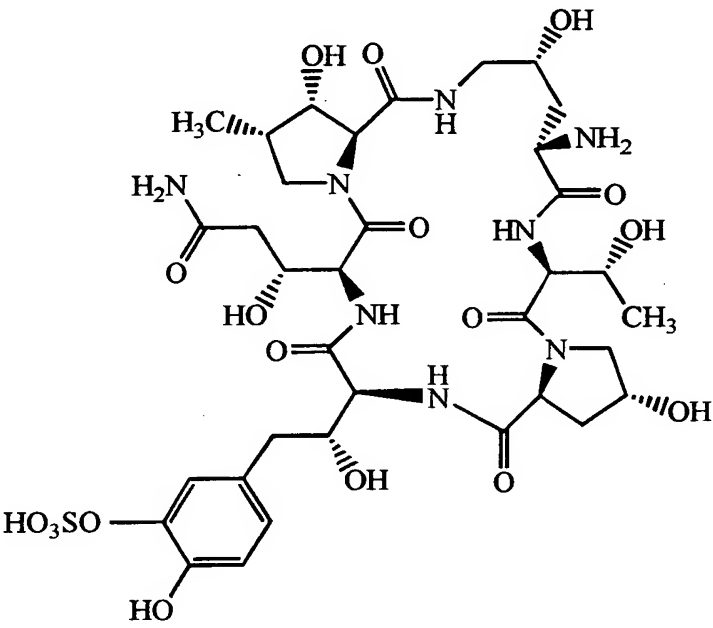
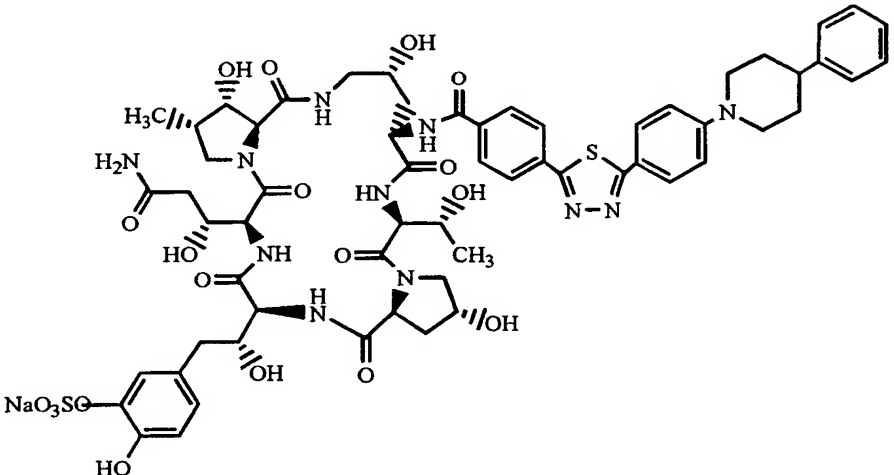
Example No.	Formula
	
111	

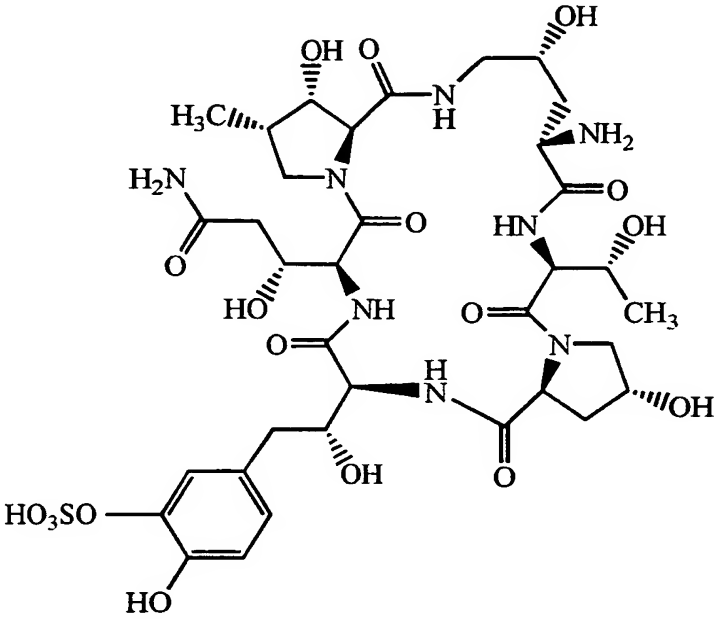
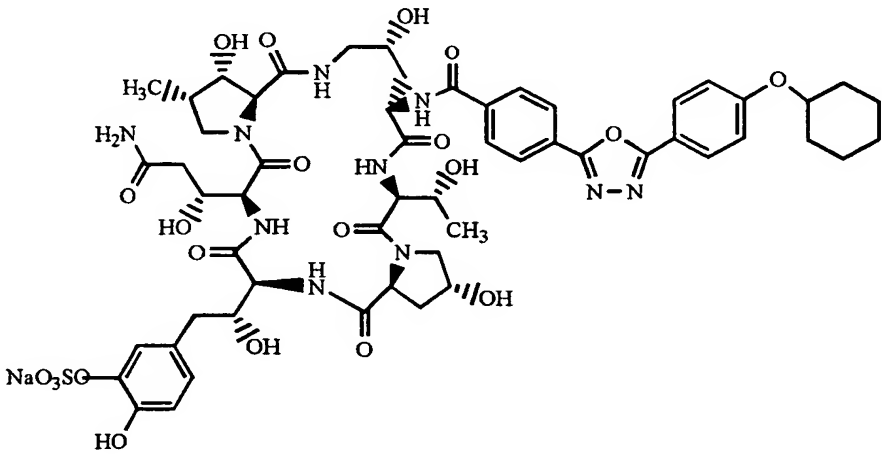
Example No.	Formula
	 <p>The structure is a complex molecule featuring several stereocenters indicated by wedges and dashes. It includes a 3-sulfamoylphenyl group (HO<sub>3</sub>SO- and HO- on a benzene ring) connected to a chain with multiple amide bonds and hydroxyl groups. A methyl group (H<sub>3</sub>C) is attached to one of the stereocenters. The molecule is highly branched with various functional groups.</p>
112	 <p>This structure is similar to the one in the first row, but it features a different side chain. Instead of the 3-sulfamoylphenyl group, it has a 3-sulfonamoylphenyl group (NaO<sub>3</sub>SO- and HO- on a benzene ring). The side chain is more complex, including a thiazole ring system and a piperidine ring. The stereochemistry and amide bonds are consistent with the first structure.</p>

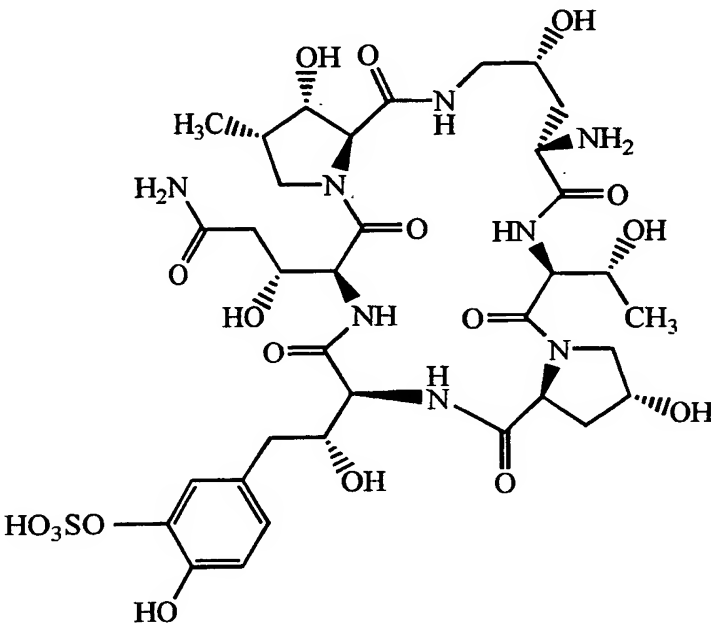
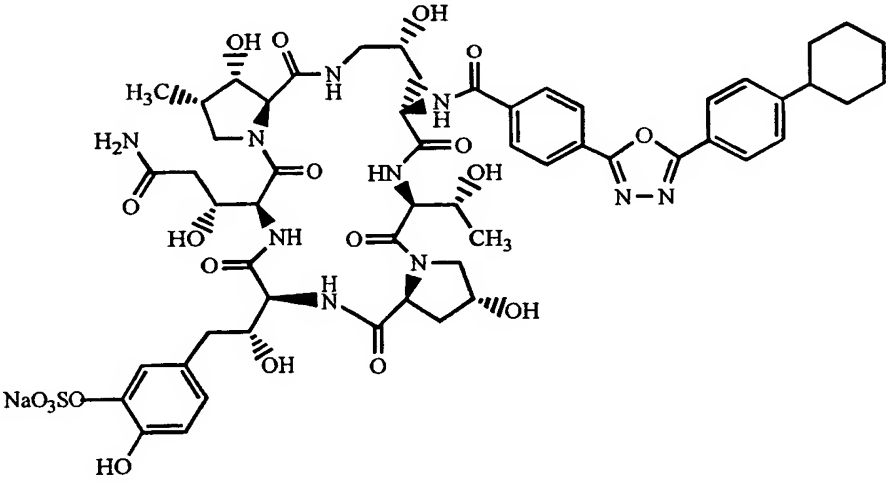


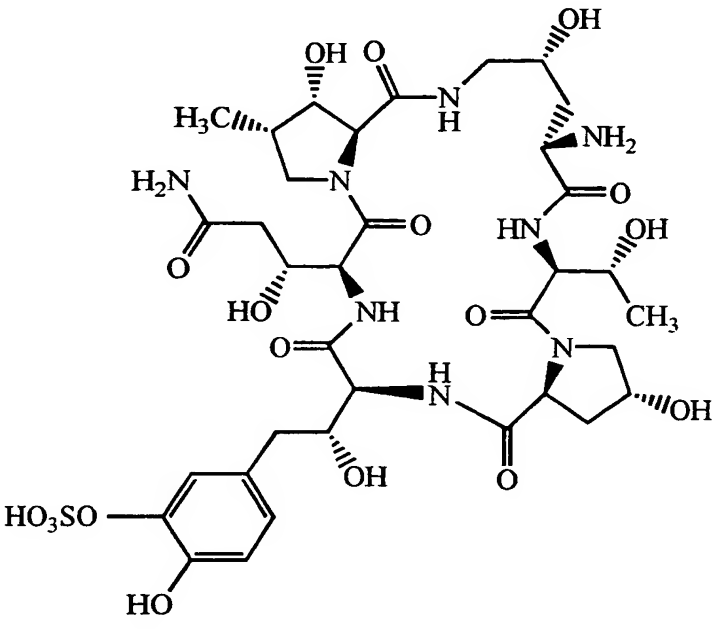
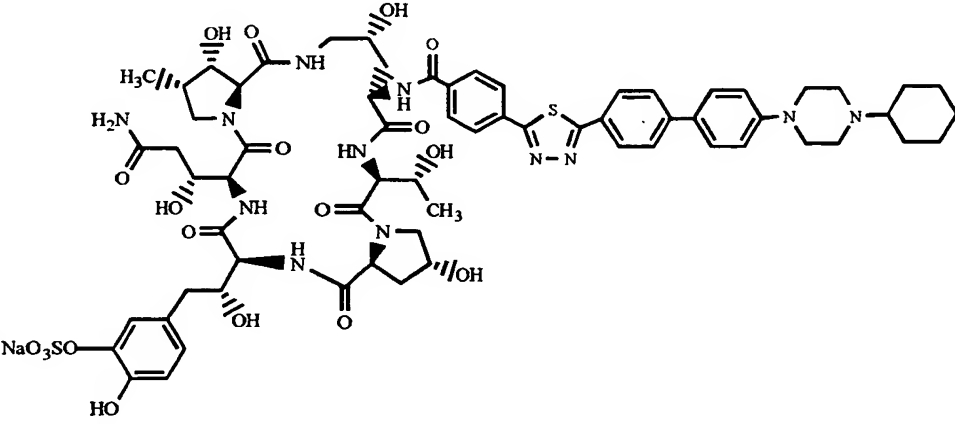
Example No.	Formula
	
113	

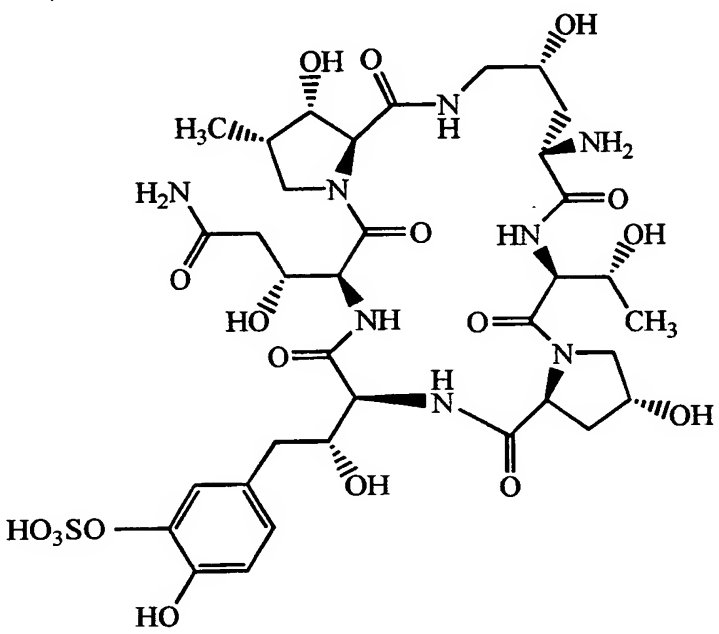
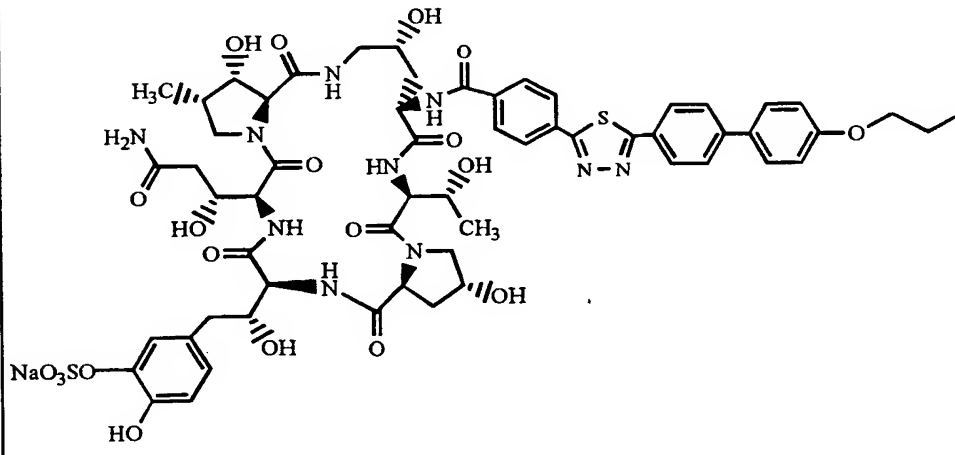
Example No.	Formula
	
114	

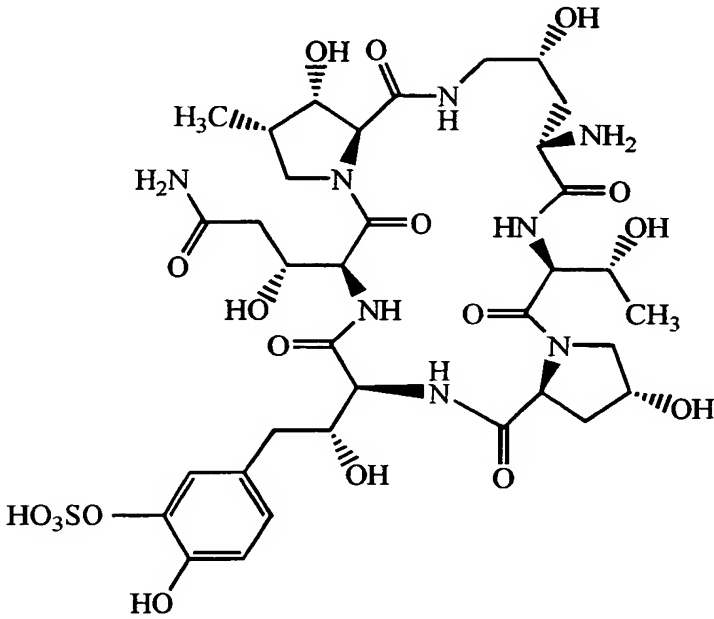
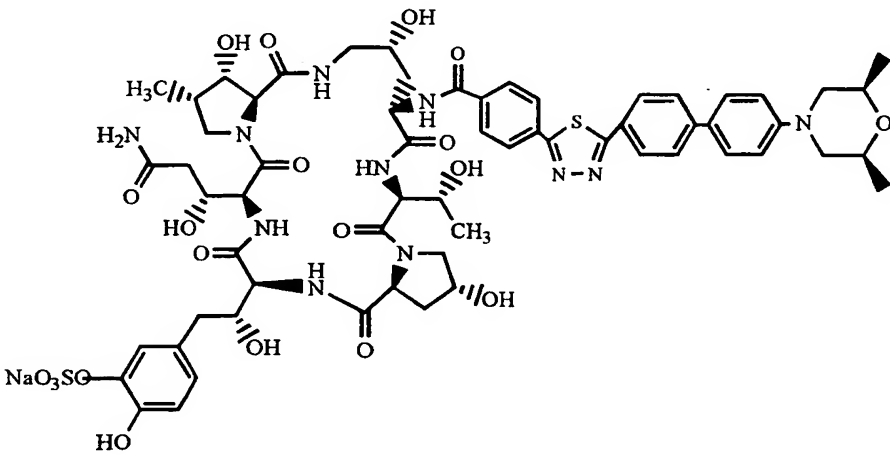
Example No.	Formula
	
115	

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfamoylphenyl group. It features a central amide linkage connecting two fragments. The left fragment includes a 4-hydroxy-3-sulfamoylphenyl group and a side chain with multiple hydroxyl and amide groups. The right fragment includes a 4-hydroxy-3-methylphenyl group and a side chain with multiple hydroxyl and amide groups.</p>
116	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfonatephenyl group. It features a central amide linkage connecting two fragments. The left fragment includes a 4-hydroxy-3-sulfonatephenyl group and a side chain with multiple hydroxyl and amide groups. The right fragment includes a 4-hydroxy-3-methylphenyl group and a side chain with multiple hydroxyl and amide groups. Additionally, there is a 4-cyclohexyloxyphenyl group connected to the right fragment via a diazo linkage.</p>

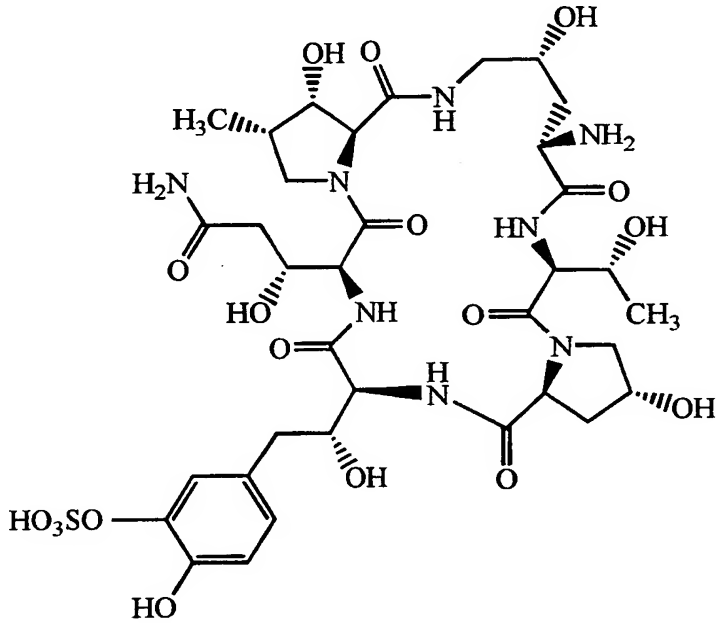
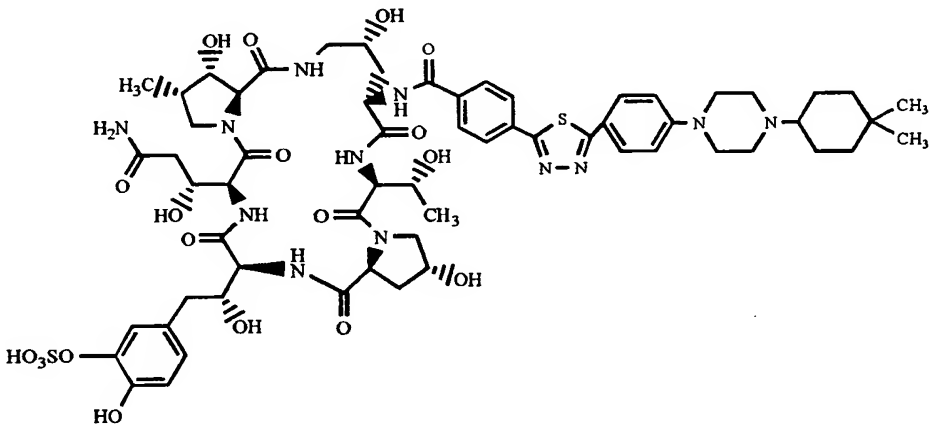
Example No.	Formula
	 <p>The structure is a complex molecule with multiple stereocenters, indicated by wedged and dashed bonds. It features several amide bonds and a 4-hydroxy-3-sulfamoylphenyl group. The molecule is composed of several interconnected rings, including a central six-membered ring and several five-membered rings, with various functional groups attached.</p>
117	 <p>The structure is a complex molecule with multiple stereocenters, indicated by wedged and dashed bonds. It features several amide bonds and a 4-hydroxy-3-sulfonatephenyl group. The molecule is composed of several interconnected rings, including a central six-membered ring and several five-membered rings, with various functional groups attached.</p>

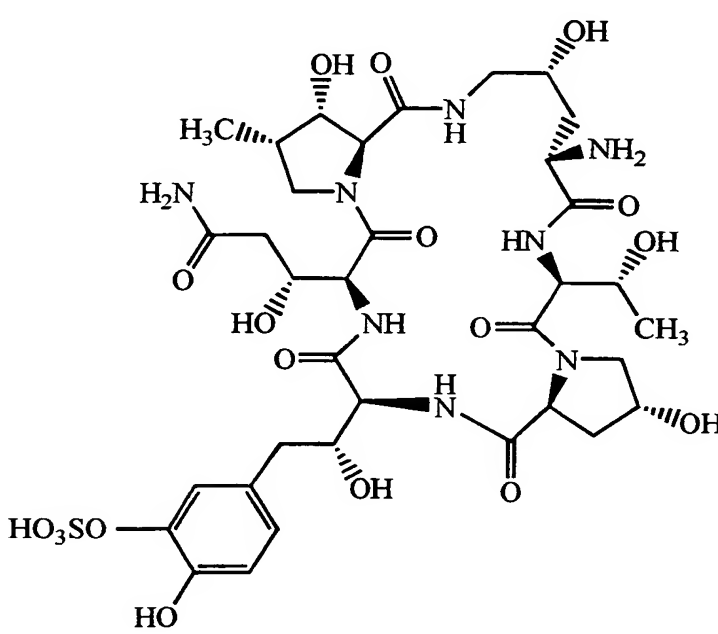
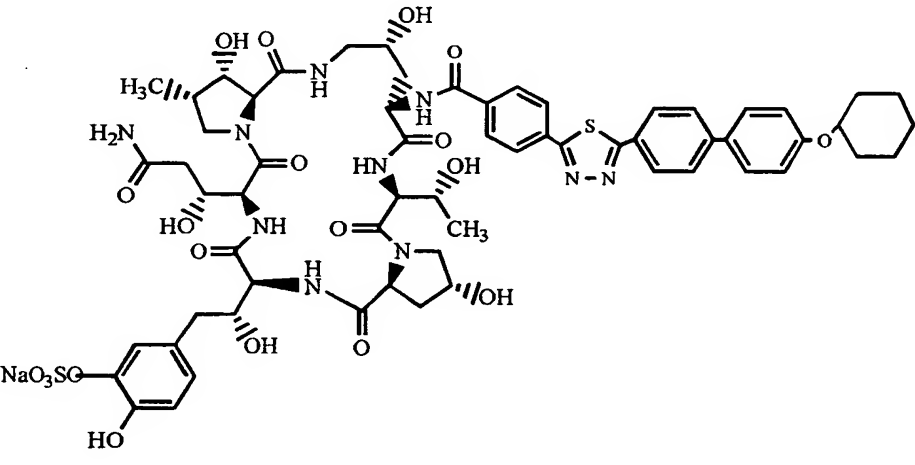
Example No.	Formula
	 <p>Chemical structure of a complex molecule. It features a central core with multiple fused and linked rings, including a p-toluenesulfonate group (HO<sub>3</sub>SO-) and a hydroxyl group (HO-). The structure is highly detailed with stereochemistry indicated by wedges and dashes.</p>
118	 <p>Chemical structure of a complex molecule, labeled 118. It features a central core with multiple fused and linked rings, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The structure is highly detailed with stereochemistry indicated by wedges and dashes.</p>

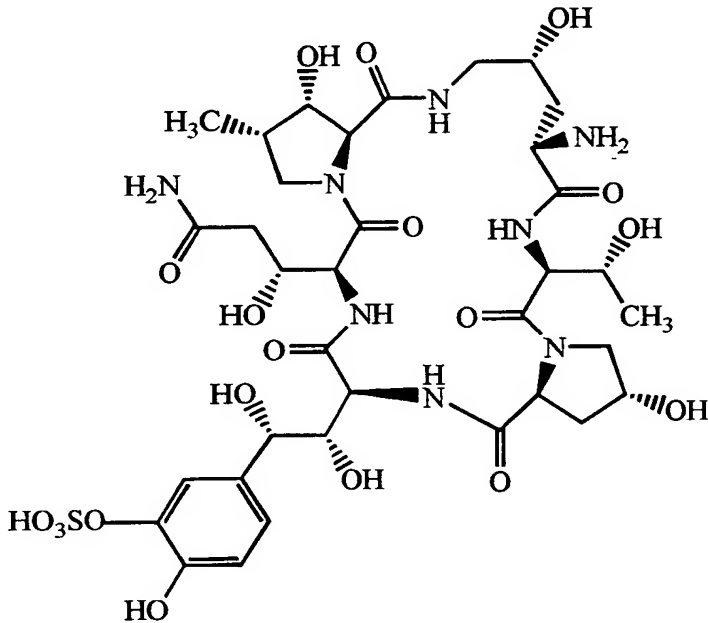
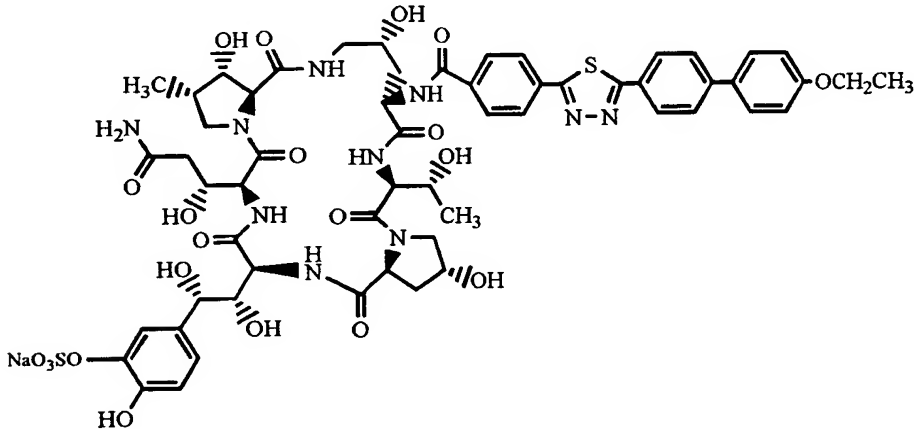
Example No.	Formula
	 <p>The structure is a complex molecule featuring several stereocenters indicated by wedges and dashes. It includes amide bonds, a 4-hydroxy-3-sulfamoylphenyl group, and a 4-hydroxy-3-methylpyrrolidine ring. The molecule is highly branched with various functional groups.</p>
119	 <p>The structure is a complex molecule, similar to the one above, but with a different substituent on the phenyl ring: a 4-hydroxy-3-sulfonatephenyl group (NaO<sub>3</sub>SO-). It also features a 4-hydroxy-3-methylpyrrolidine ring and a 4-ethoxyphenyl group connected via a triazole ring. The molecule has multiple stereocenters indicated by wedges and dashes.</p>

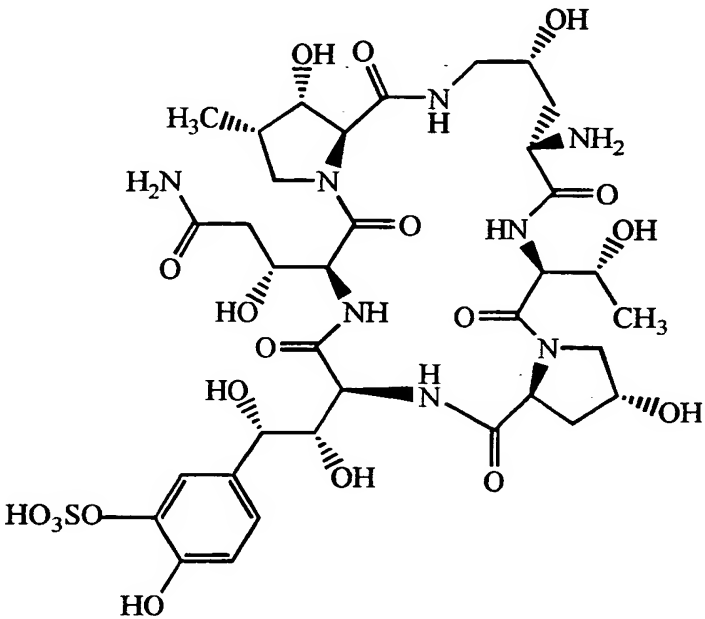
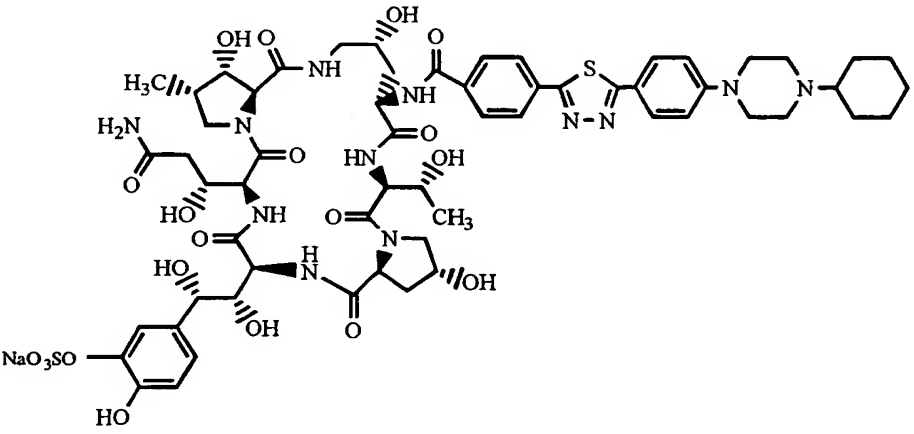
Example No.	Formula
120	
	

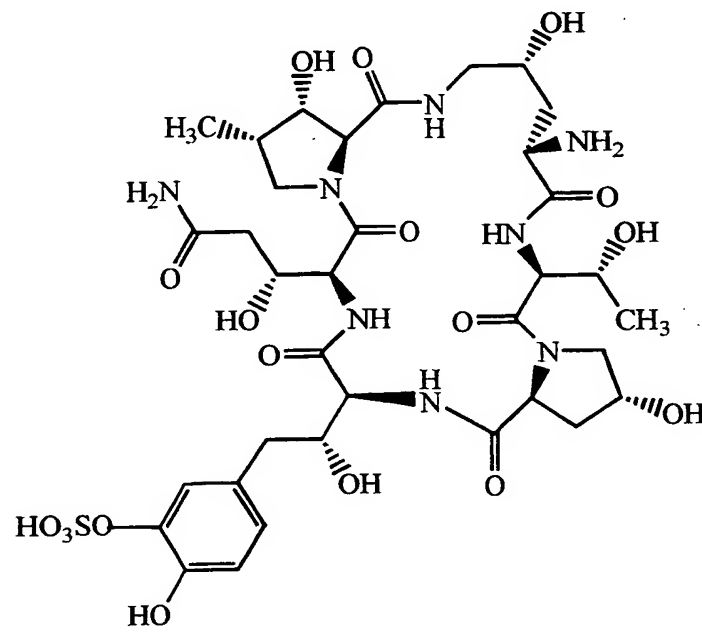
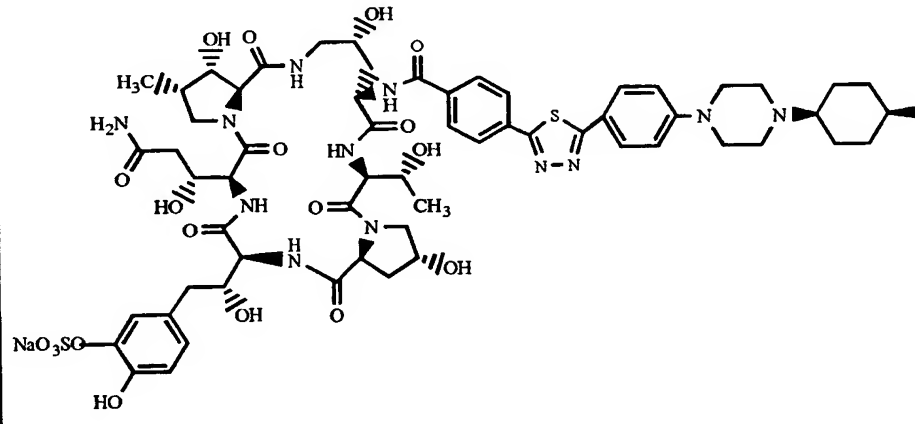


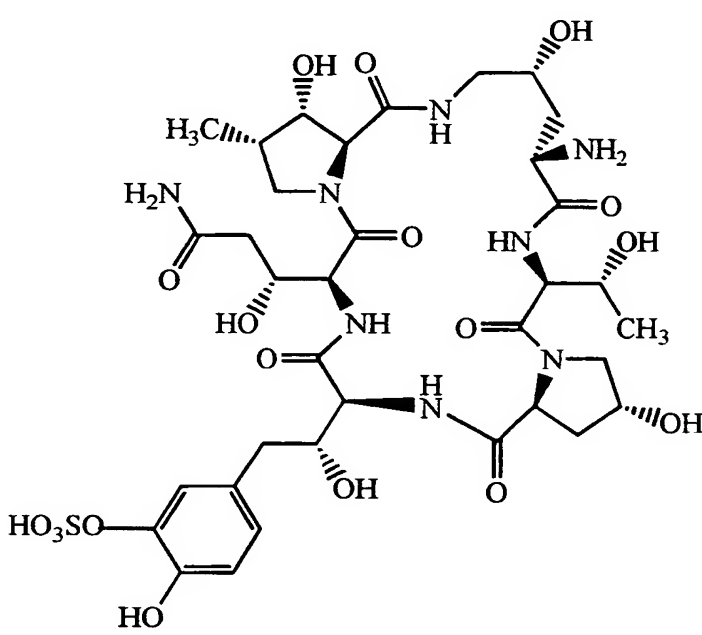
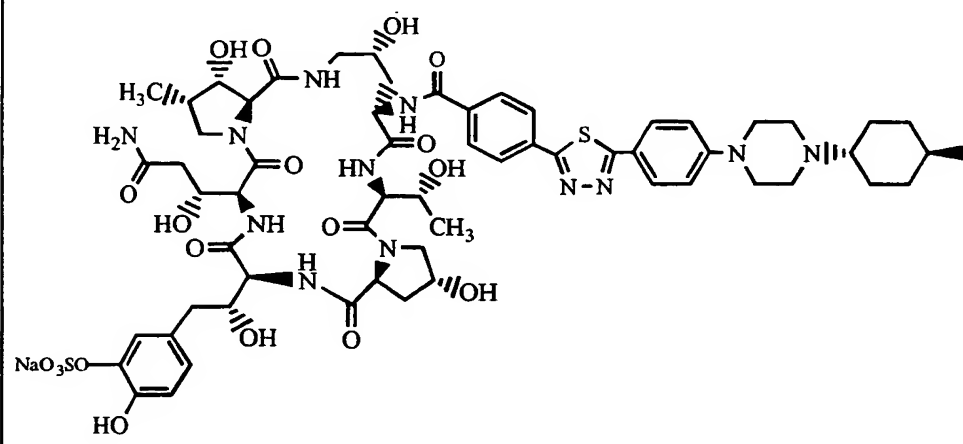
Example No.	Formula
	
121	

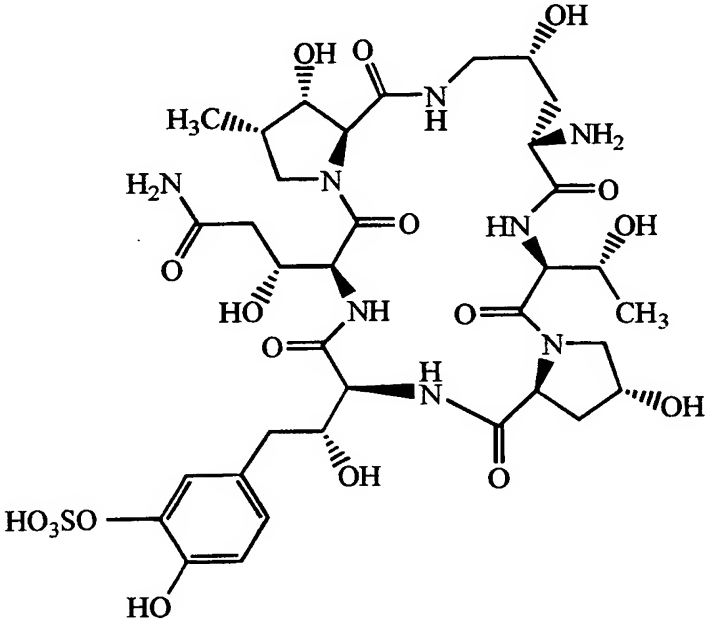
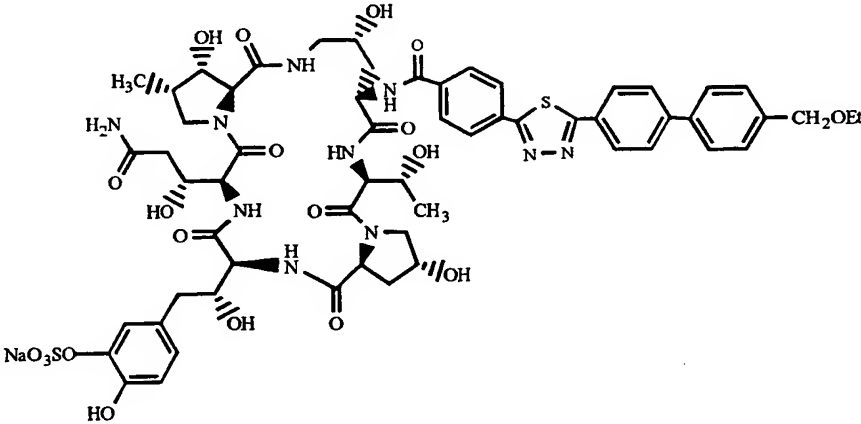
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central amide linkage connecting two side chains. One side chain includes a sulfonamide group (HO<sub>3</sub>SO-) and a hydroxyl group (HO-). The other side chain includes a methyl group (H<sub>3</sub>C) and a hydroxyl group (OH). The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds.</p>
122	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central amide linkage connecting two side chains. One side chain includes a sulfonamide group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The other side chain includes a methyl group (CH<sub>3</sub>) and a hydroxyl group (OH). The molecule is highly branched and contains several chiral centers indicated by wedged and dashed bonds. Additionally, there is a long chain with a sulfonamide group (S-N-N) and a hydroxyl group (OH) extending from the central amide linkage.</p>

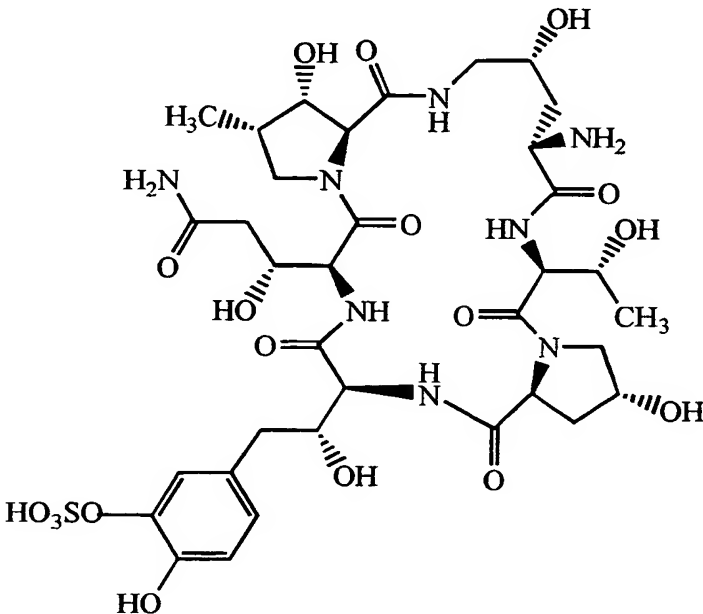
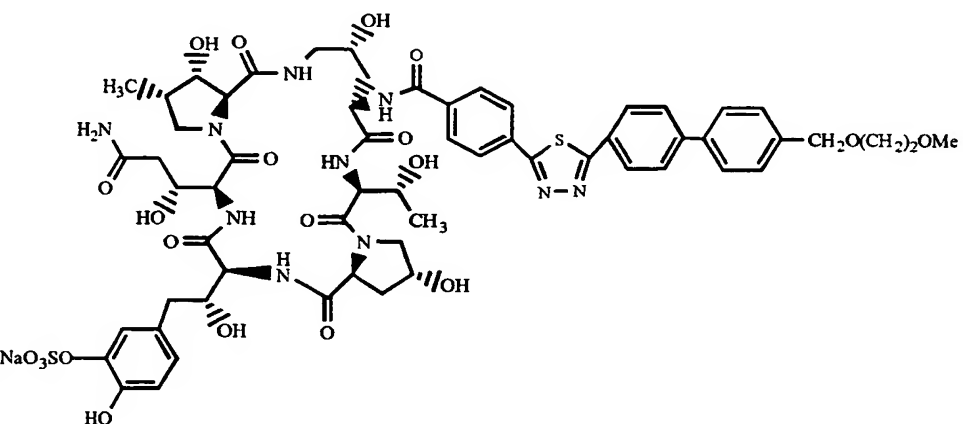
Example No.	Formula
	
123	

Example No.	Formula
	 <p>The structure is a complex molecule with multiple stereocenters, indicated by wedged and dashed bonds. It features several amide bonds and a 4-hydroxy-3-sulfonatephenyl group. The molecule is highly branched and contains various functional groups including hydroxyl, amine, and amide.</p>
124	 <p>The structure is a complex molecule with multiple stereocenters, indicated by wedged and dashed bonds. It features several amide bonds and a 4-hydroxy-3-sulfonatephenyl group. The molecule is highly branched and contains various functional groups including hydroxyl, amine, and amide. A sodium sulfonate group (NaO<sub>3</sub>SO) is present on the phenyl ring.</p>

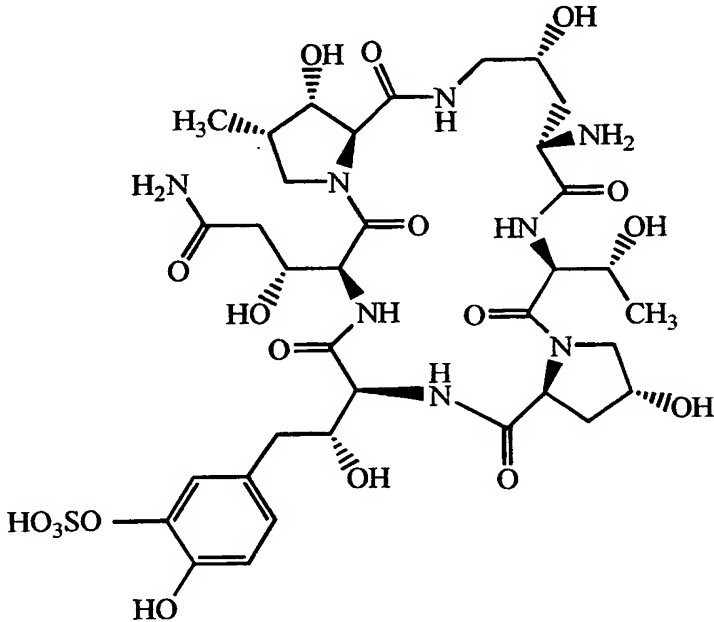
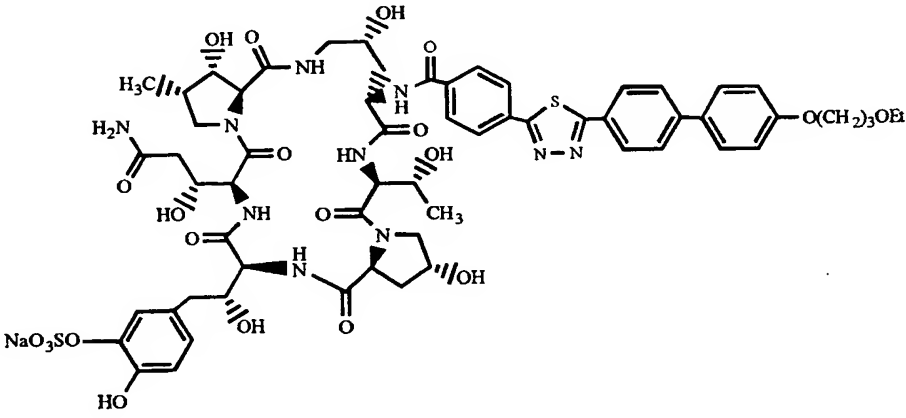
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfamoylphenyl group. It features a central amide linkage connecting two chiral fragments. One fragment includes a 4-hydroxy-3-sulfamoylphenyl group, and the other includes a 4-hydroxy-3-methylphenyl group. The molecule is highly stereoselective, with various chiral centers indicated by wedges and dashes.</p>
125	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfonatephenyl group. It features a central amide linkage connecting two chiral fragments. One fragment includes a 4-hydroxy-3-sulfonatephenyl group, and the other includes a 4-hydroxy-3-methylphenyl group. The molecule is highly stereoselective, with various chiral centers indicated by wedges and dashes.</p>

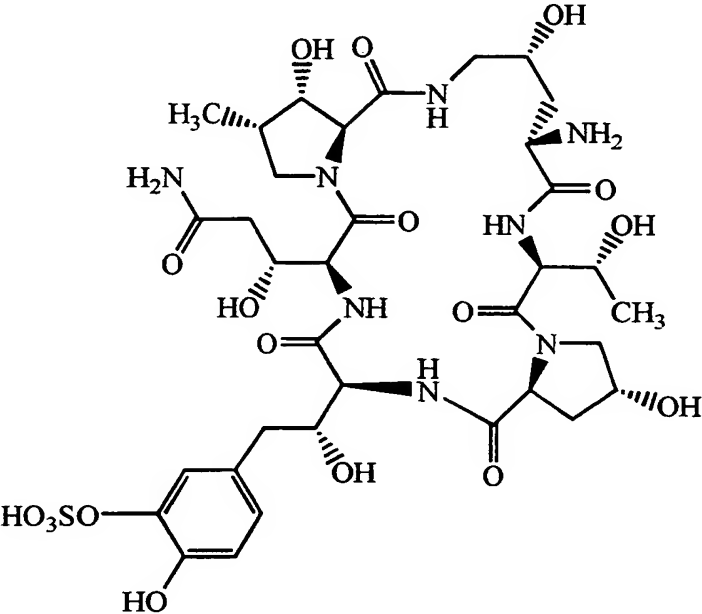
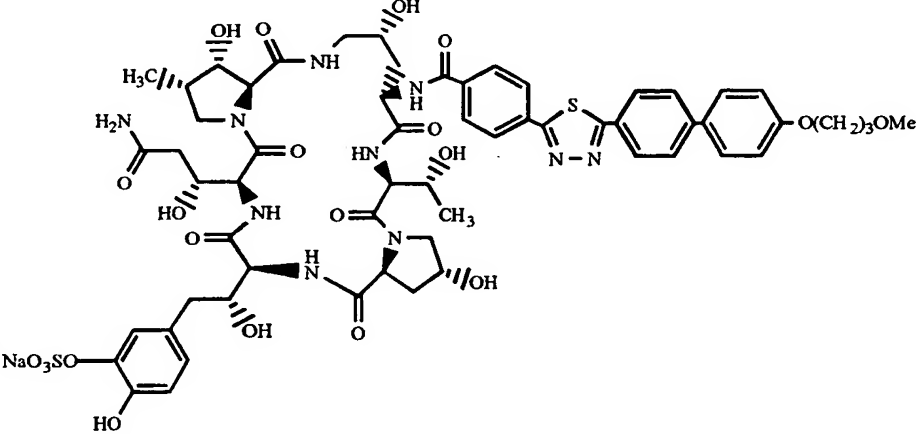
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a 4-hydroxy-3-sulfonatephenyl substituent. The molecule is composed of several interconnected rings and functional groups, including a sulfonate group (HO<sub>3</sub>SO-), a hydroxyl group (HO-), and various amide and ester linkages.</p>
126	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a 4-hydroxy-3-sulfonatephenyl substituent, with a sodium salt (NaO<sub>3</sub>SO-) indicated. The molecule is composed of several interconnected rings and functional groups, including a sulfonate group (NaO<sub>3</sub>SO-), a hydroxyl group (HO-), and various amide and ester linkages.</p>

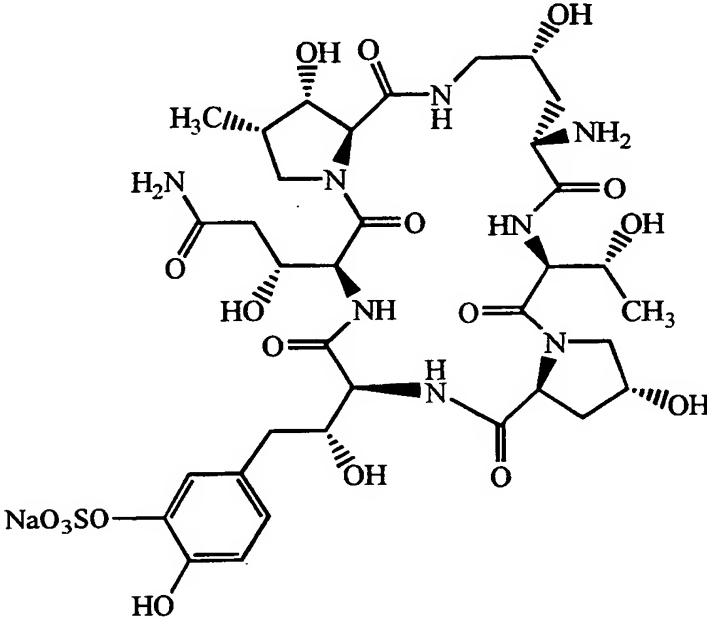
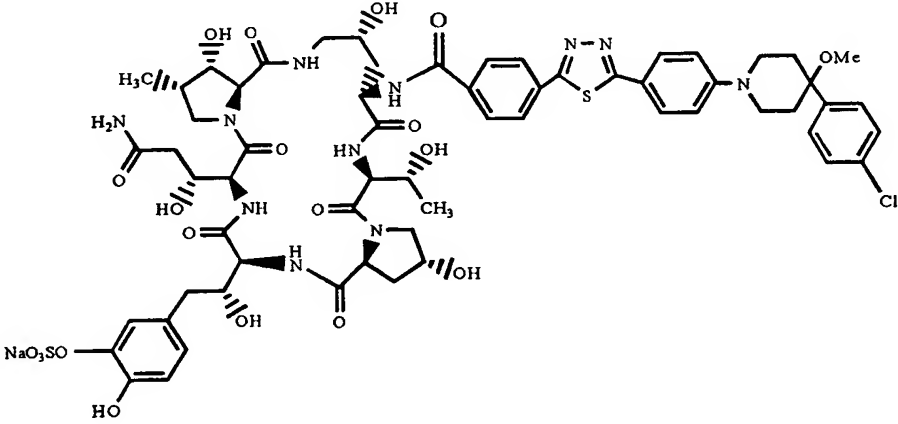
Example No.	Formula
	
127	

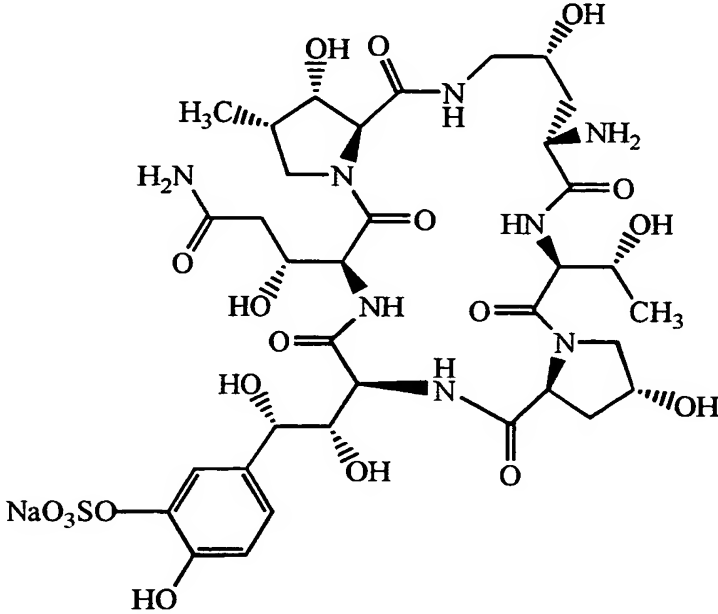
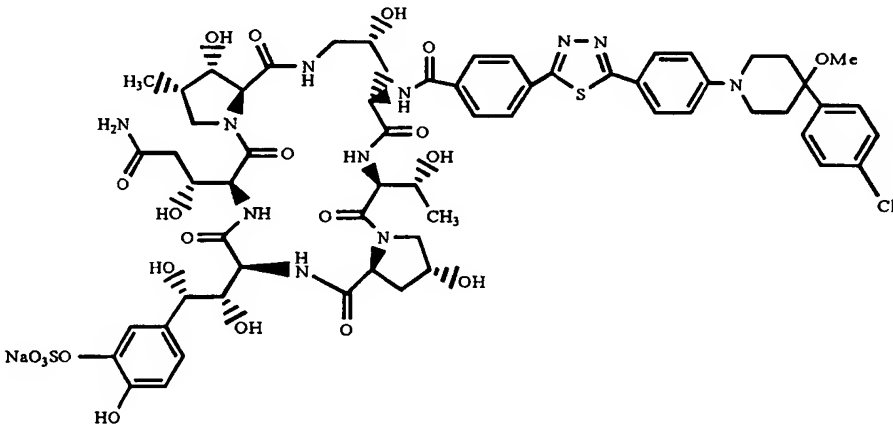
Example No.	Formula
	 <p>The structure is a complex polycyclic molecule. It features a central core with several stereocenters indicated by wedges and dashes. Key functional groups include amide bonds, hydroxyl groups, a methyl group, and a 3-sulfamoyl-4-hydroxyphenyl substituent. The molecule is highly symmetrical in its connectivity.</p>
128	 <p>This structure is similar to the one in the first row, but it has a different side chain. It features a 4-(2-methoxyethoxy)phenyl group connected to a thiazole ring, which is further connected to the main polycyclic core. Additionally, it has a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group on a phenyl ring. The stereochemistry is also indicated with wedges and dashes.</p>

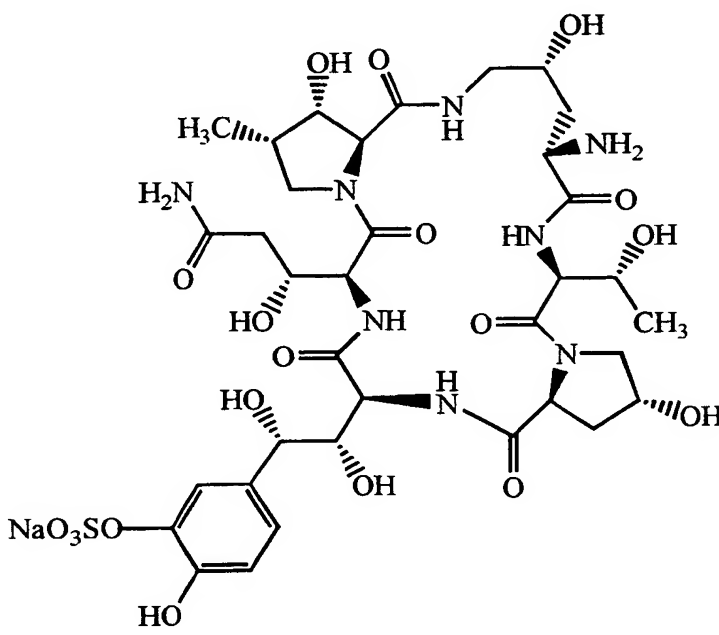
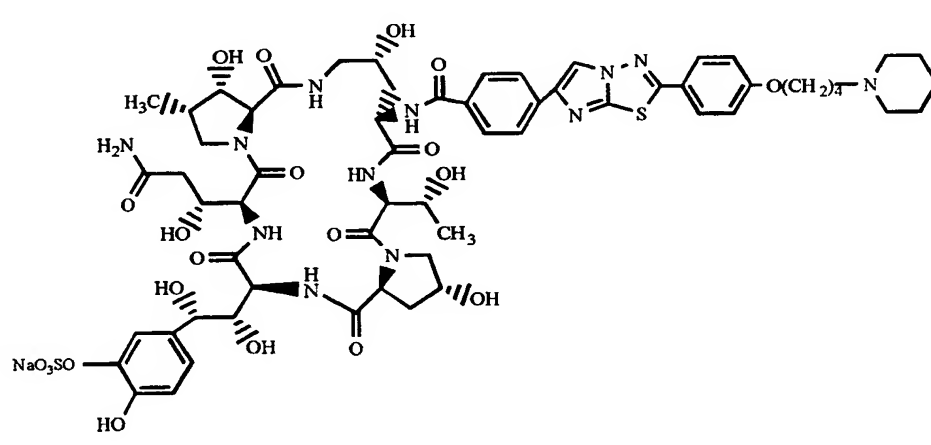


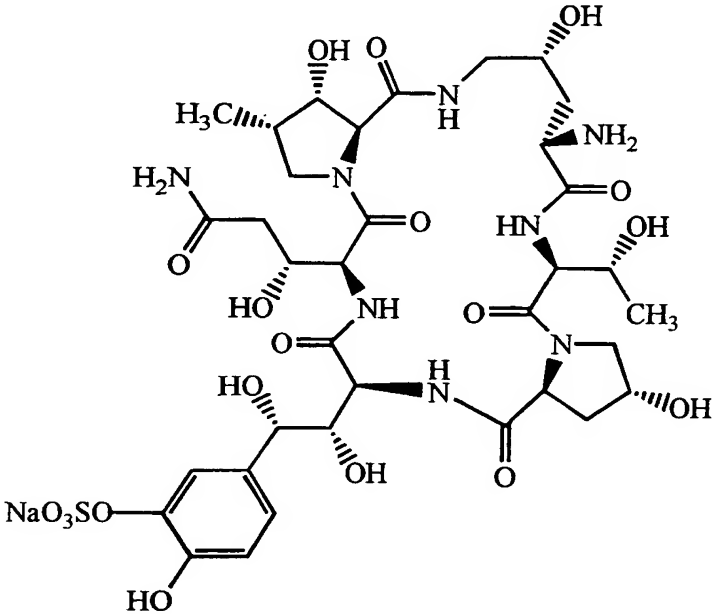
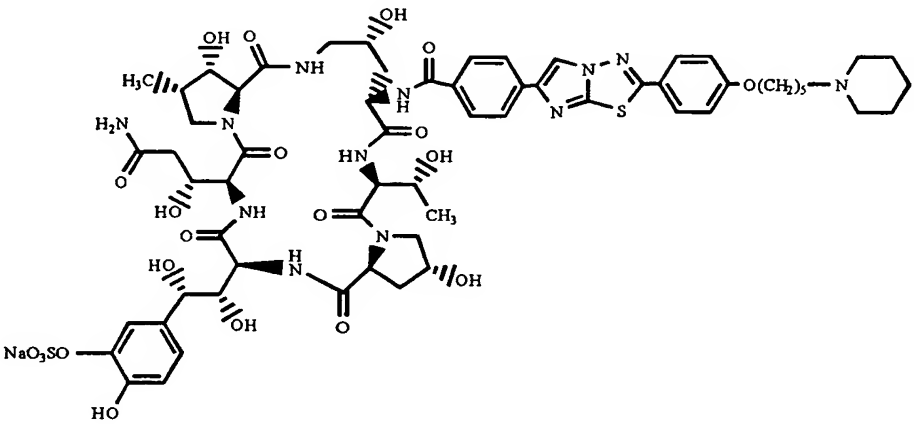
Example No.	Formula
	
129	

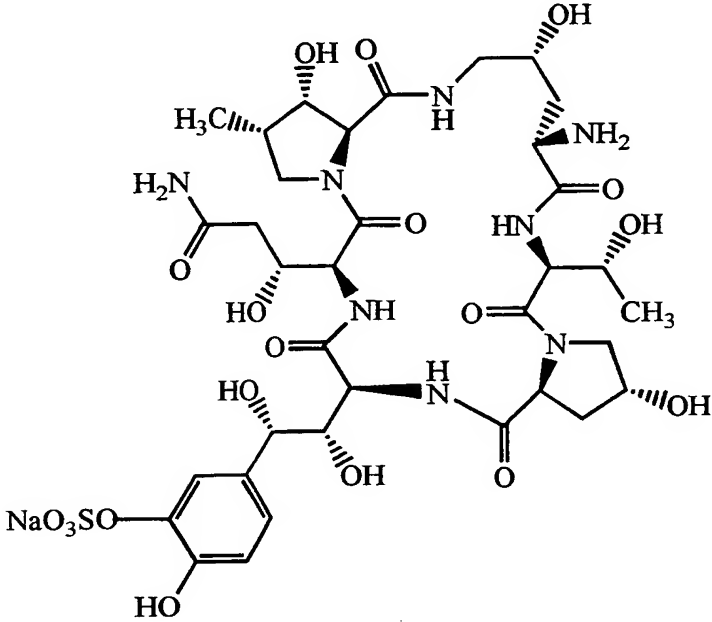
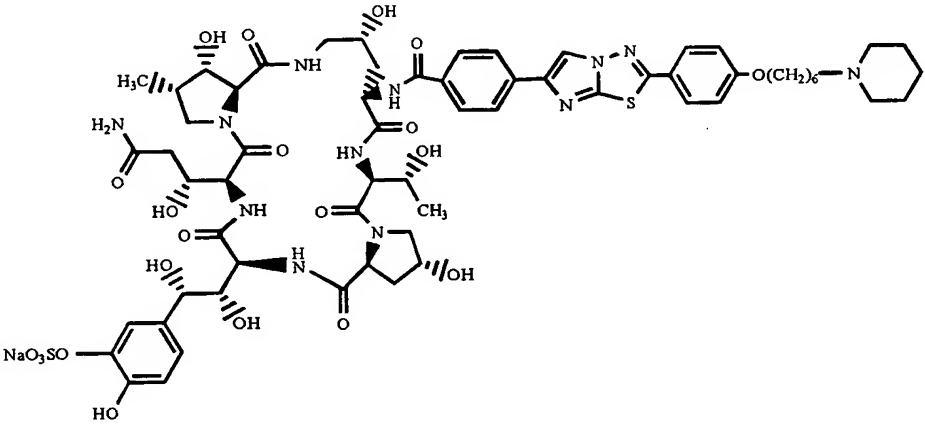
Example No.	Formula
	
130	

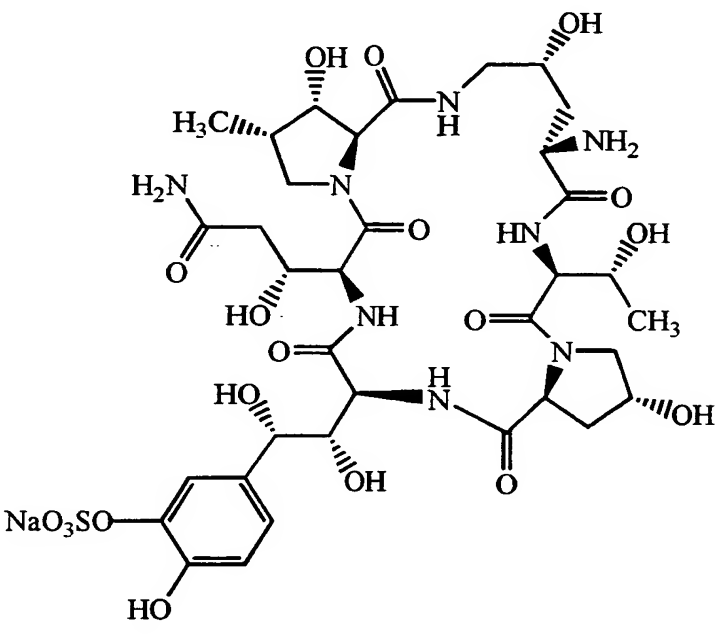
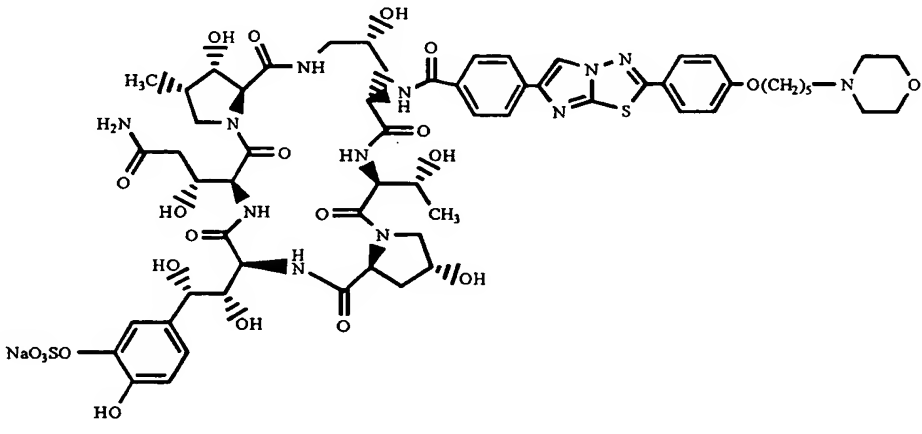
Example No.	Formula
	
131	

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. The molecule is composed of several interconnected rings and functional groups, including a sulfonate group (NaO<sub>3</sub>SO-), a hydroxyl group (HO-), and a methyl group (H<sub>3</sub>C-).</p>
132	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. The molecule is composed of several interconnected rings and functional groups, including a sulfonate group (NaO<sub>3</sub>SO-), a hydroxyl group (HO-), a methyl group (H<sub>3</sub>C-), a thiazole ring, and a methoxy group (OMe).</p>

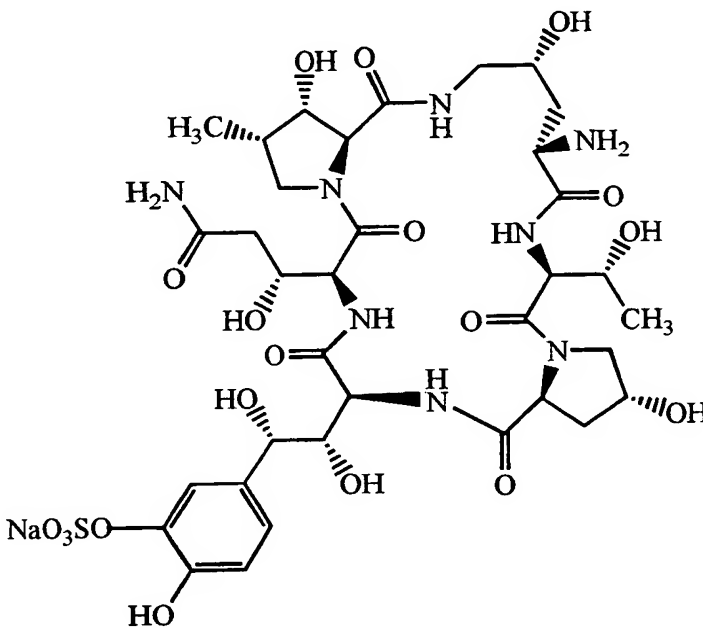
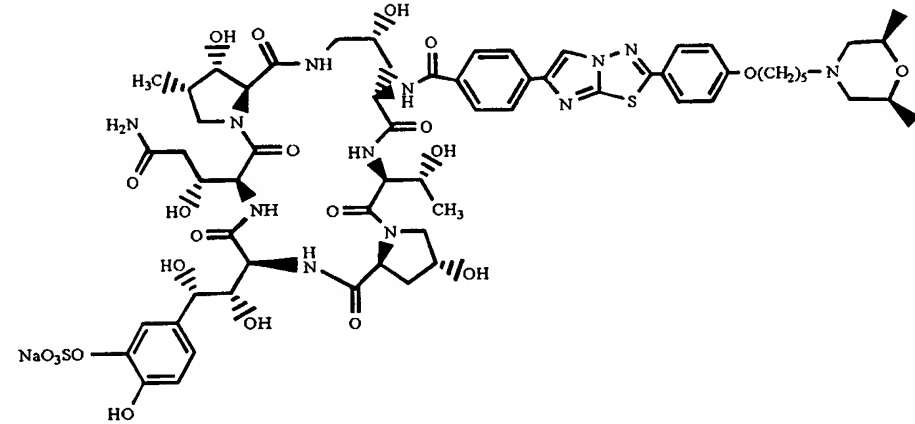
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group. It features a central amide linkage connecting two chiral fragments. One fragment includes a pyrrolidine ring with a methyl group and a hydroxyl group, and another includes a piperidine ring with a hydroxyl group. The molecule is terminated by a 4-hydroxyphenyl group with a sodium sulfonate group.</p>
133	 <p>This structure is similar to the one above, but the side chain is different. It features a thiazole ring connected to a piperidine ring via a linker. The molecule also contains a 4-hydroxyphenyl group with a sodium sulfonate group and a complex amide backbone with multiple stereocenters.</p>

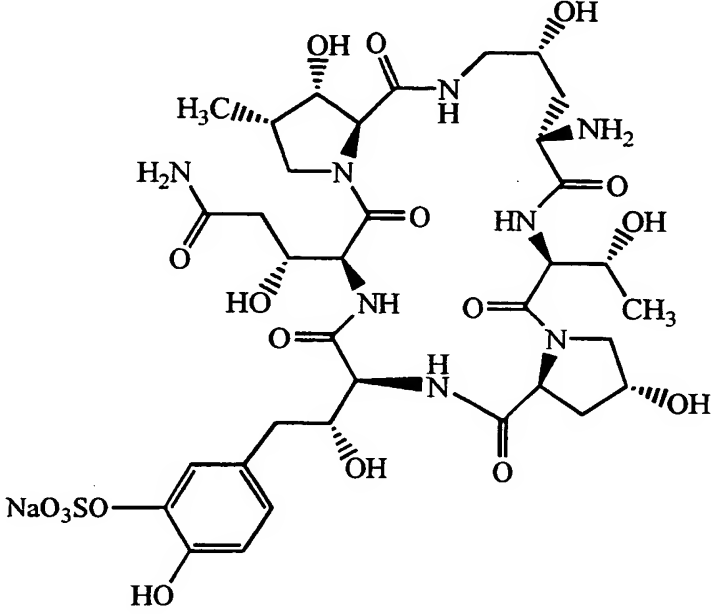
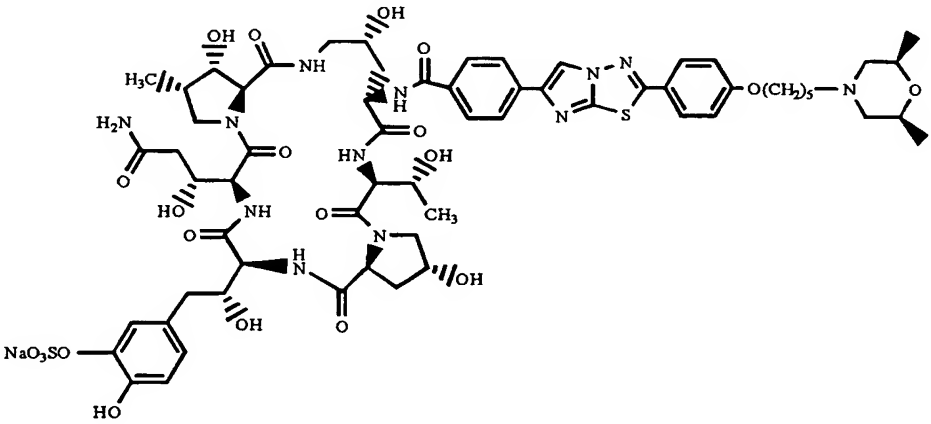
Example No.	Formula
134	 <p>Chemical structure of a complex molecule, likely a peptide derivative, featuring multiple stereocenters, amide bonds, and a 4-hydroxyphenyl group. The structure includes a sulfonate group (NaO<sub>3</sub>SO-) and a methyl group (CH<sub>3</sub>).</p>
	 <p>Chemical structure of a complex molecule, similar to the one above, but featuring a long alkoxy chain (O(CH<sub>2</sub>)<sub>5</sub>N) and a different side chain (a benzimidazole derivative).</p>

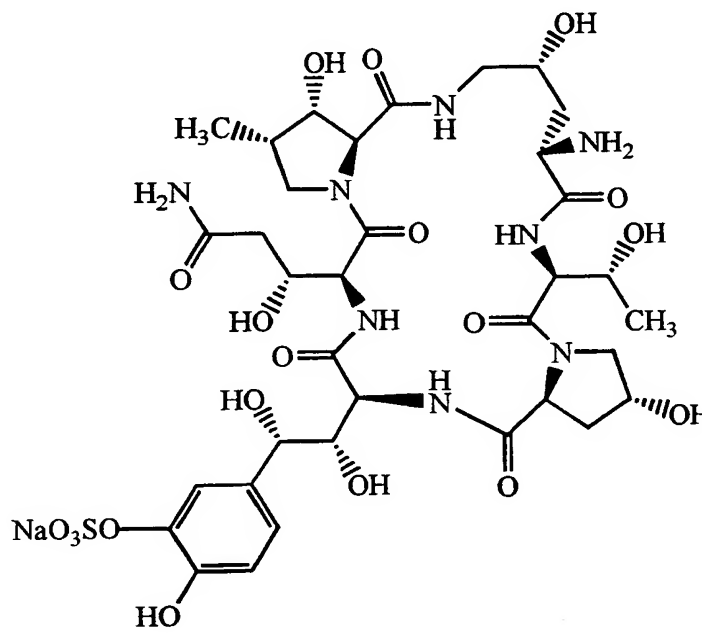
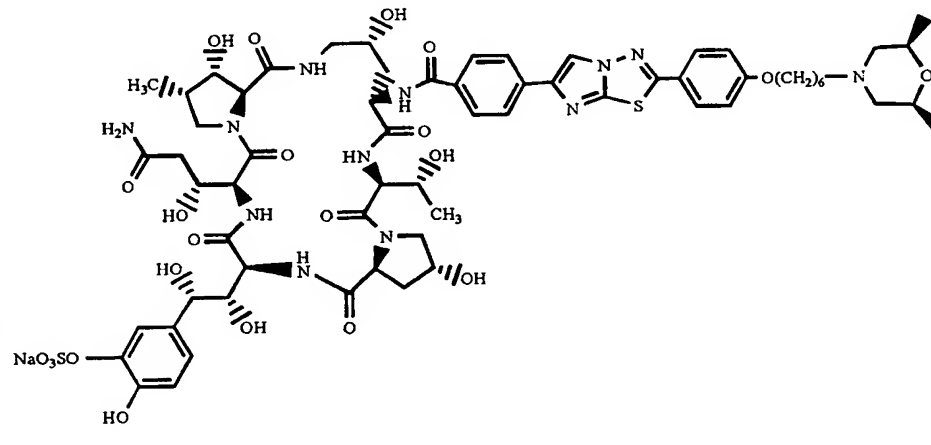
Example No.	Formula
	
135	

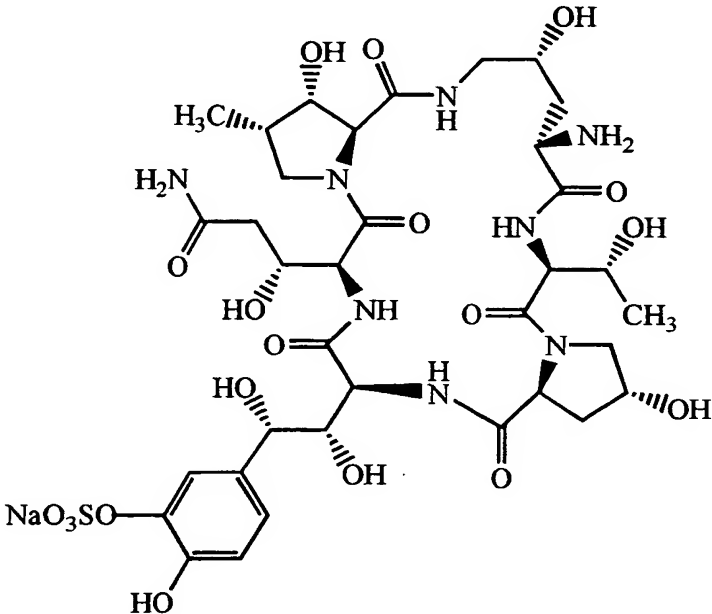
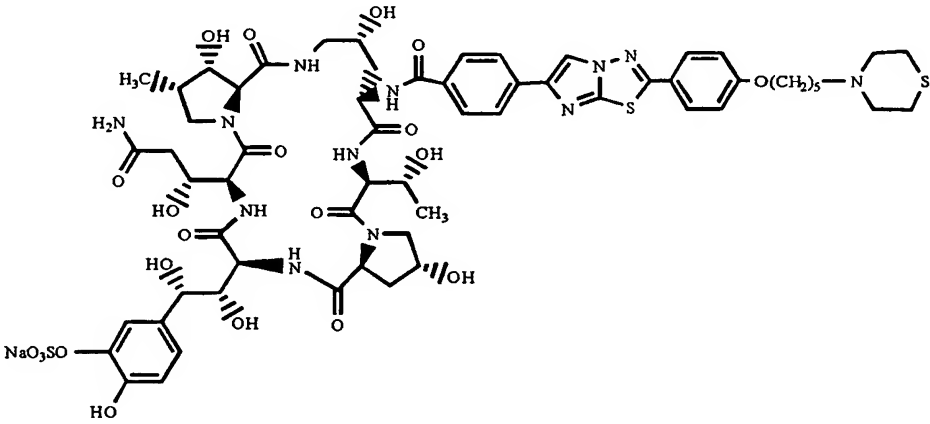
Example No.	Formula
	 <p>Chemical structure of a complex molecule. It features a central core with multiple fused and linked rings, including a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The structure is highly detailed with stereochemistry indicated by wedges and dashes.</p>
136	 <p>Chemical structure of a complex molecule, labeled 136. It features a central core with multiple fused and linked rings, including a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The structure is highly detailed with stereochemistry indicated by wedges and dashes.</p>

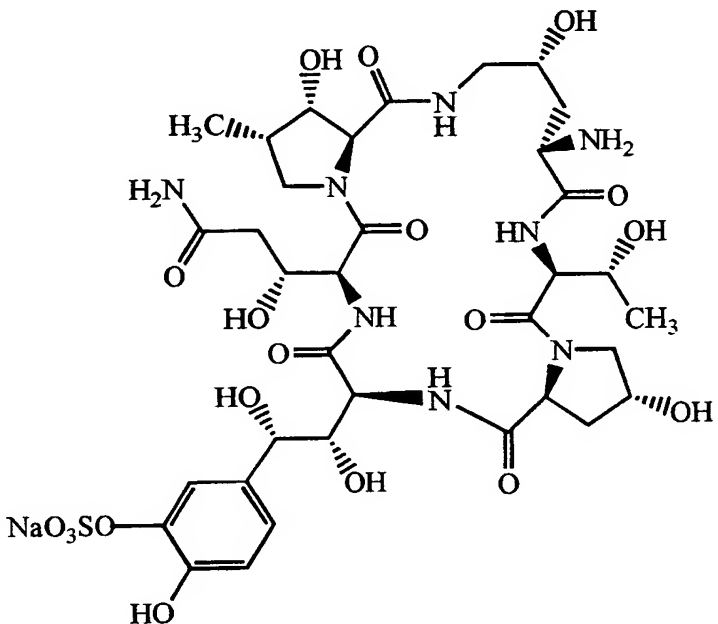
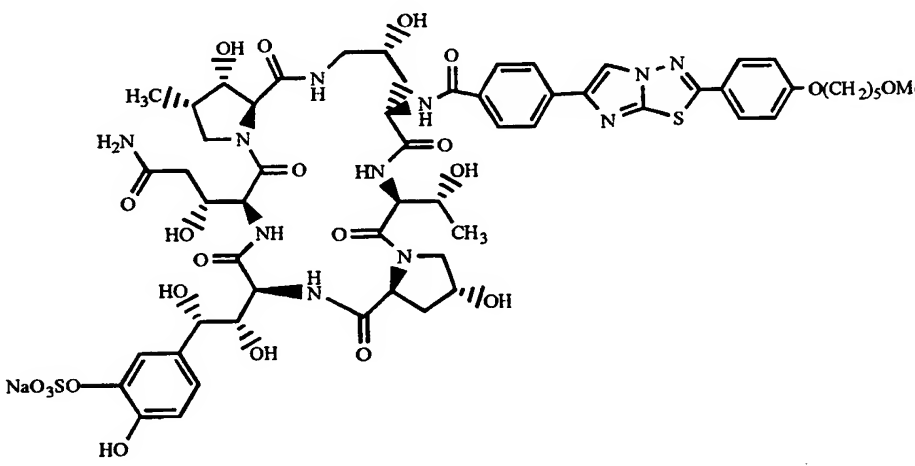


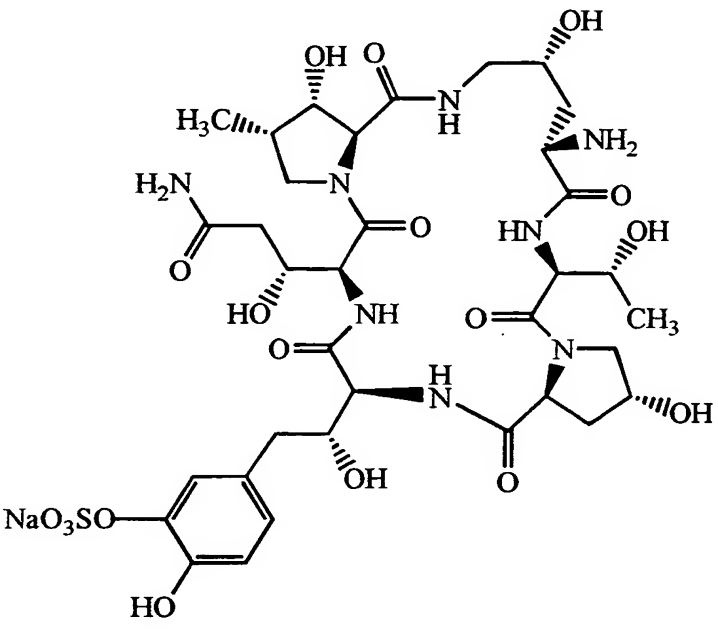
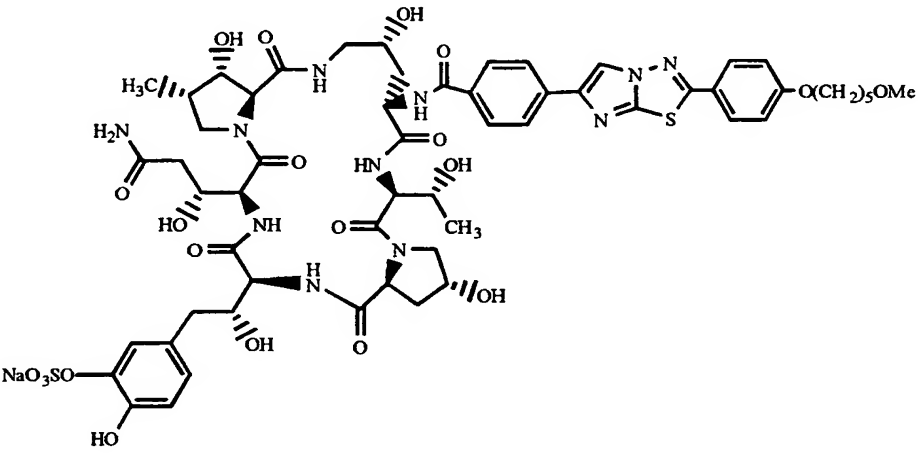
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various substituents, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
137	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various substituents, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>

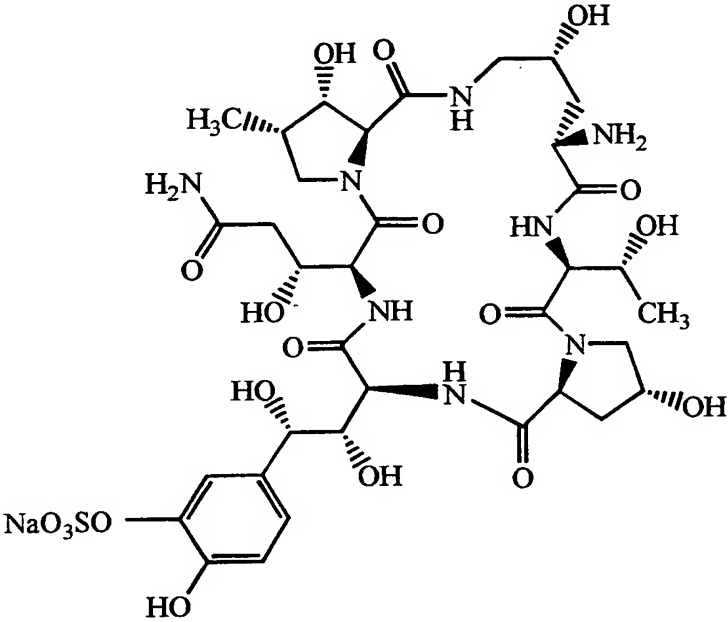
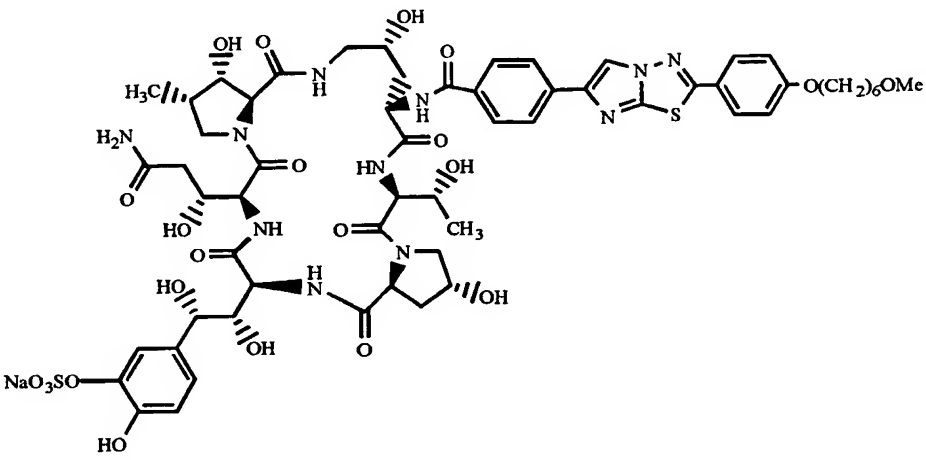
Example No.	Formula
	
138	

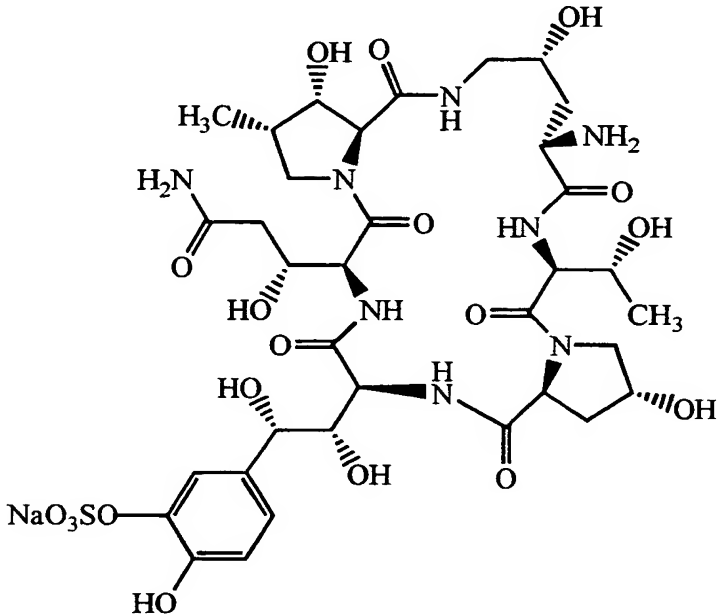
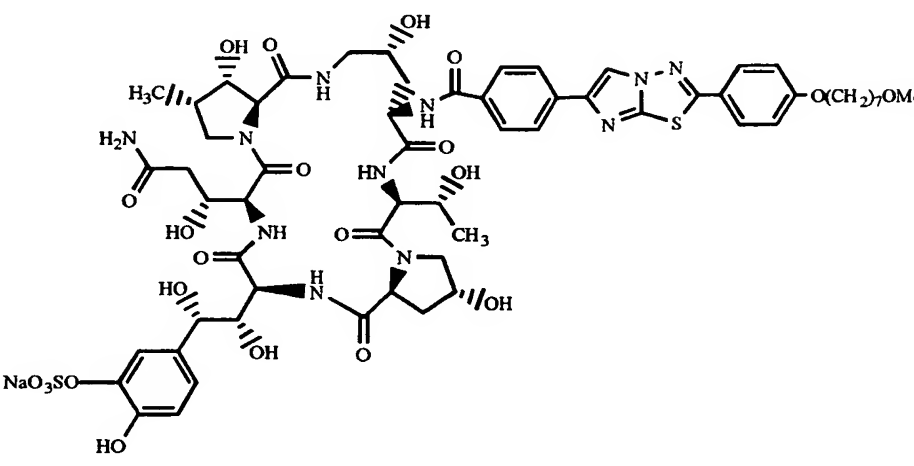
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group.</p>
139	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxyphenyl group with a sodium sulfonate group, featuring a long linker with a thiazole ring and a morpholine derivative.</p>

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. It includes a central amide linkage connecting two fragments, one of which has a methyl group and a hydroxyl group, and the other has a hydroxyl group and a methyl group. The 3-hydroxy-4-sulfonatophenyl group is attached to a chiral center.</p>
140	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. It includes a central amide linkage connecting two fragments, one of which has a methyl group and a hydroxyl group, and the other has a hydroxyl group and a methyl group. The 3-hydroxy-4-sulfonatophenyl group is attached to a chiral center. A long chain with a thiazole ring and a thiomorpholine group is also present.</p>

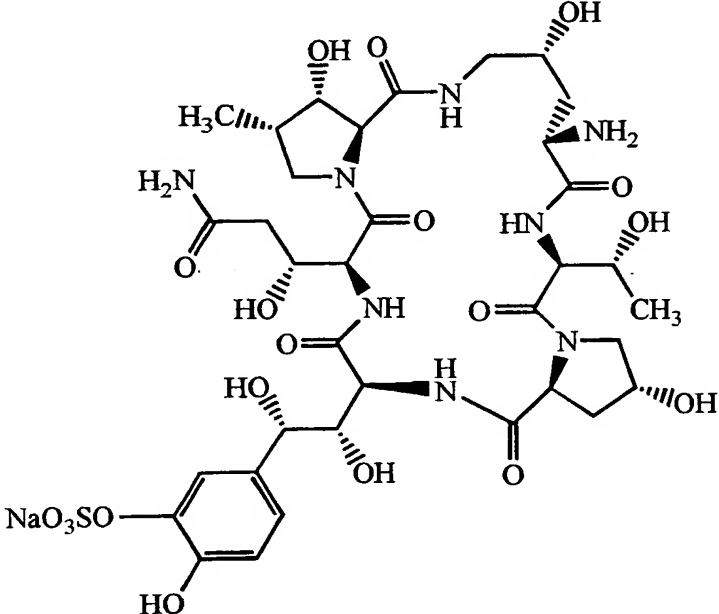
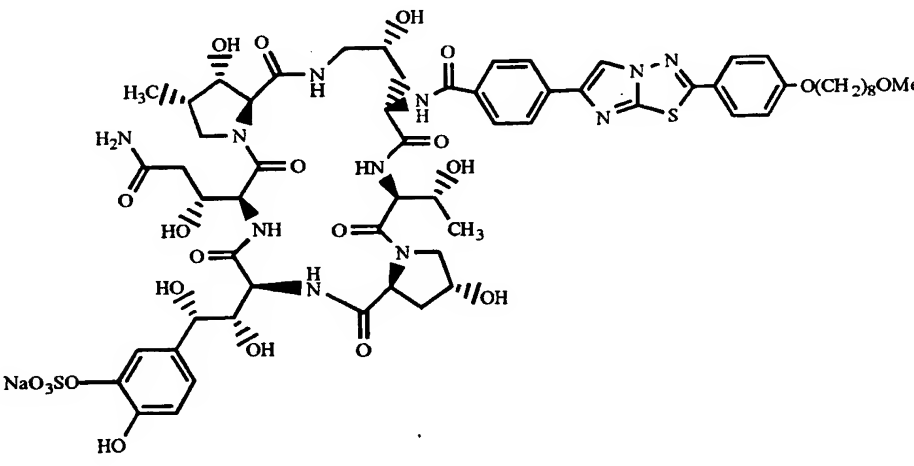
Example No.	Formula
	 <p>Chemical structure of a complex molecule. It features a central core with multiple fused and linked rings, including a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The structure is highly detailed with stereochemistry indicated by wedges and dashes.</p>
141	 <p>Chemical structure of a complex molecule, similar to the one above but with a different side chain. It features a central core with multiple fused and linked rings, including a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The side chain is more complex, involving a benzene ring and a thiazole ring system.</p>

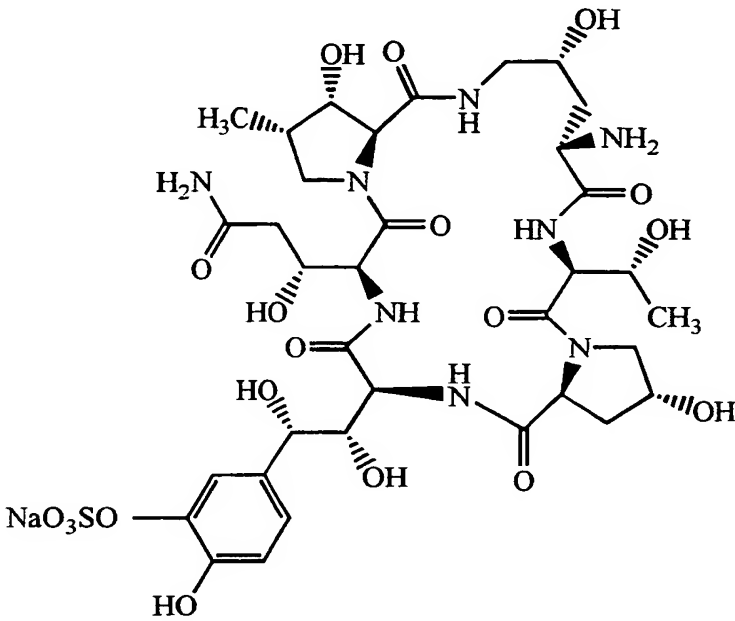
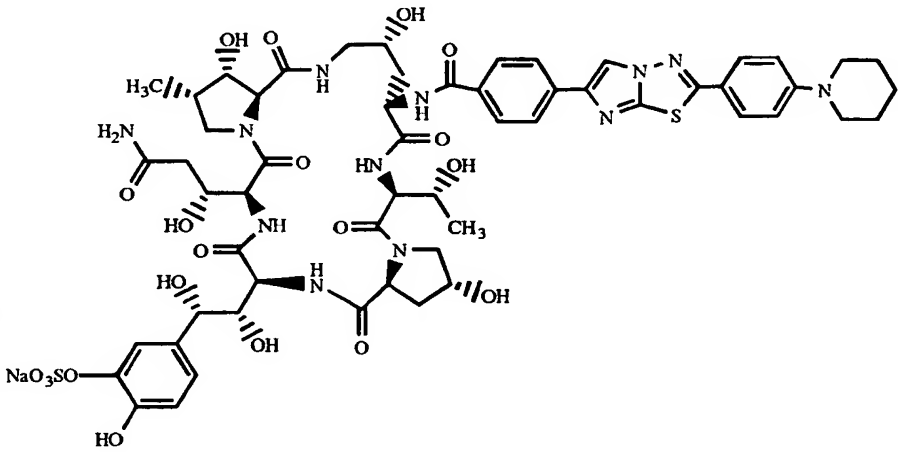
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a sodium sulfonate group. It features a central core with various substituents, including a hydroxyl group, a methyl group, and a sodium sulfonate group.</p>
142	 <p>The structure is similar to the one above but with a different side chain. It features a central core with various substituents, including a hydroxyl group, a methyl group, and a sodium sulfonate group. The side chain is more complex, featuring a triazole ring and a methoxy group.</p>

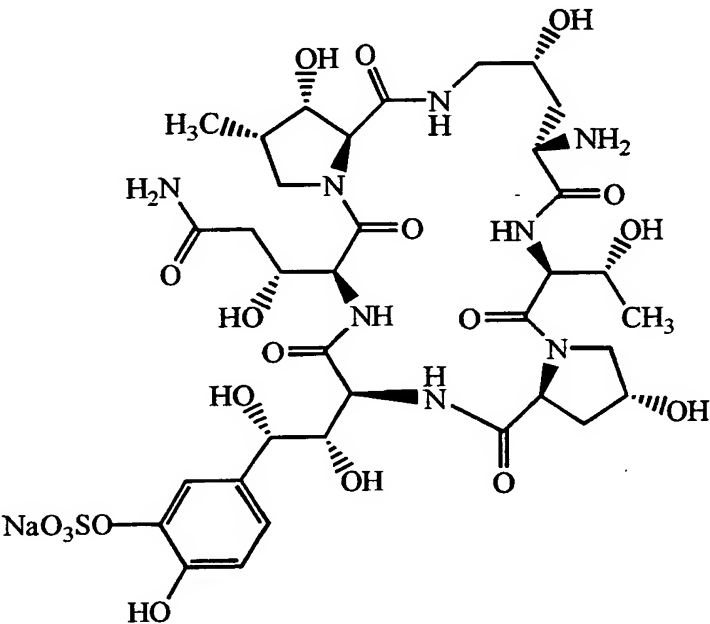
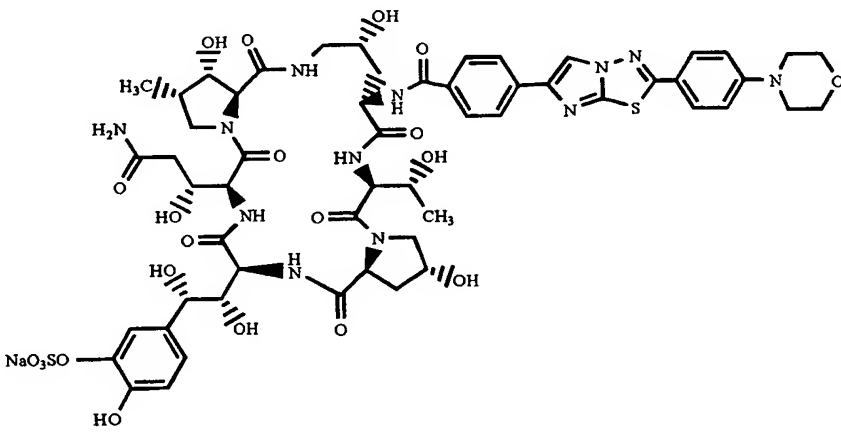
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. The sulfonate group is represented as NaO<sub>3</sub>SO.</p>
143	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. The sulfonate group is represented as NaO<sub>3</sub>SO. A long alkoxy chain is present, represented as O(CH<sub>2</sub>)<sub>6</sub>OMe.</p>

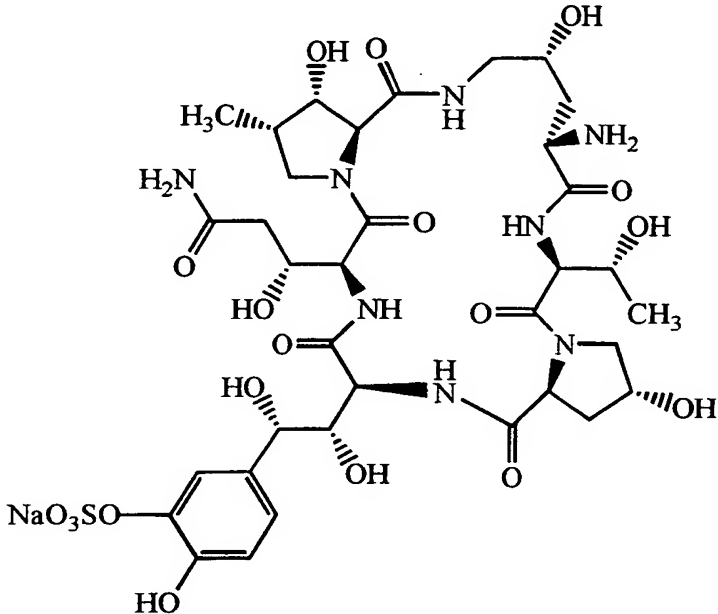
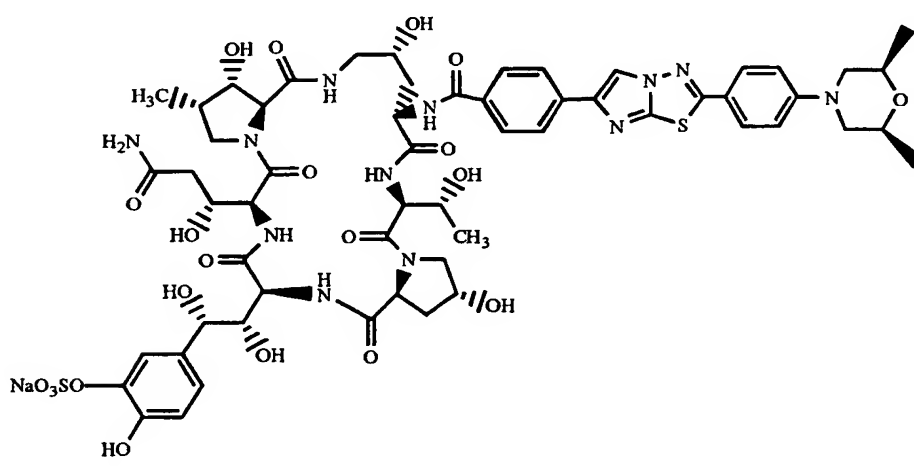
Example No.	Formula
	
144	

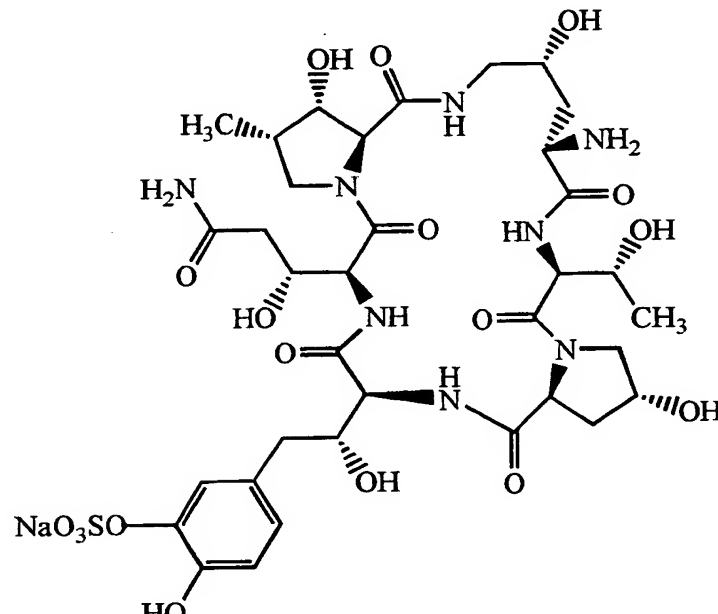
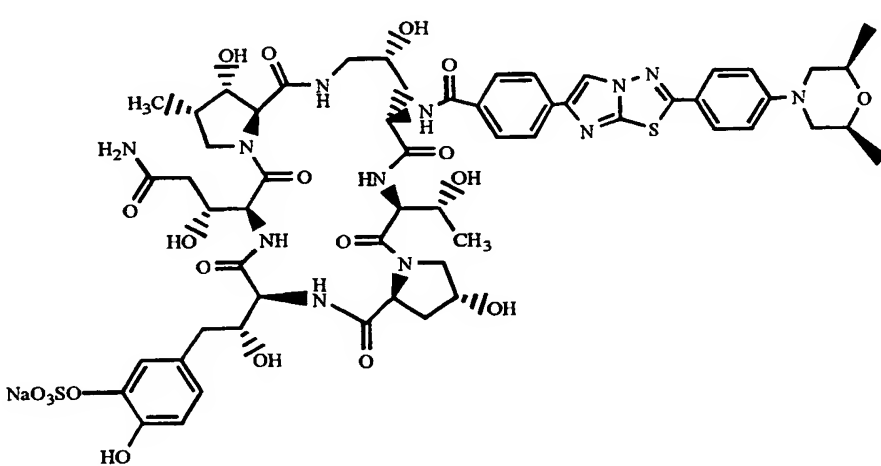


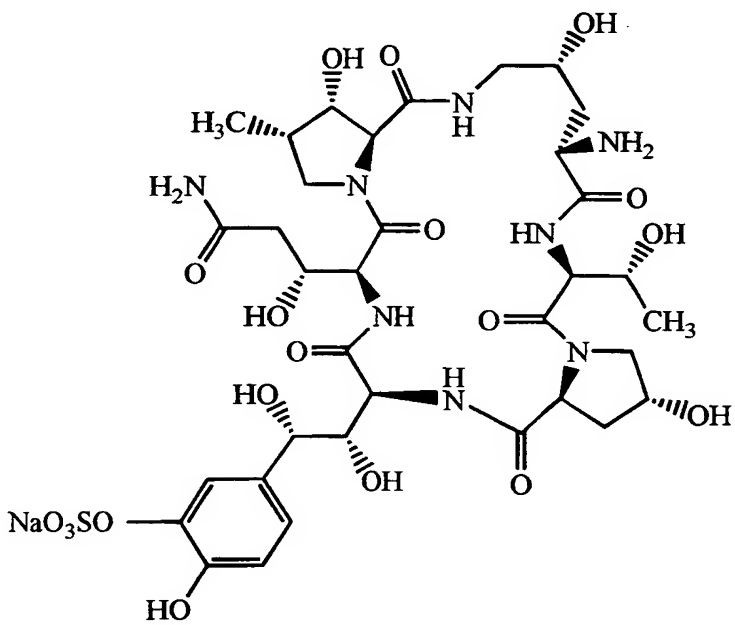
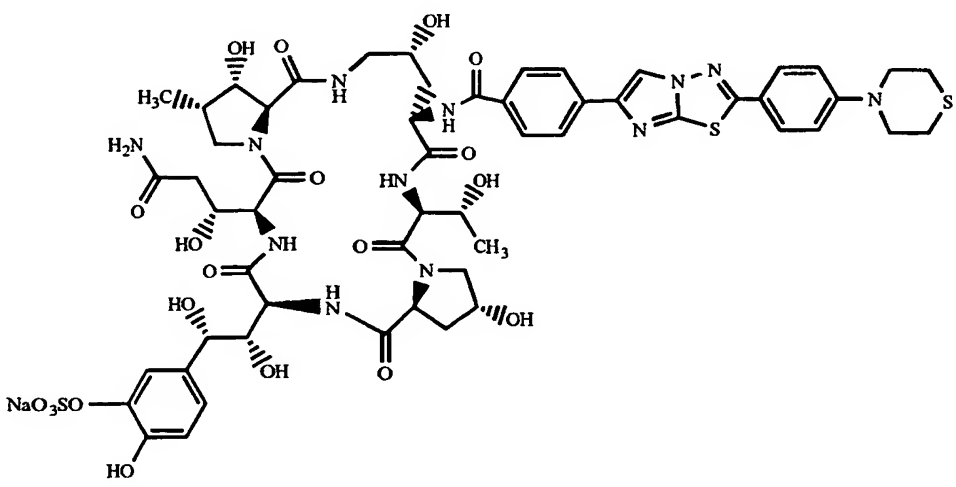
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple fused and linked rings. It includes a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several amide and ester linkages.</p>
145	 <p>The structure shows a complex molecule with multiple fused and linked rings. It includes a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule is highly branched and contains several amide and ester linkages. It also features a long alkoxy chain (O(CH<sub>2</sub>)<sub>8</sub>OMe) and a thiazole ring system.</p>

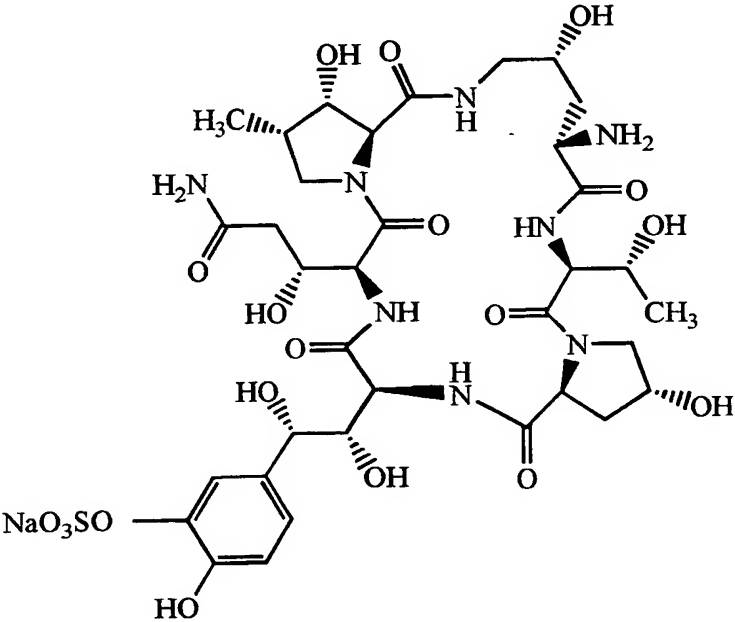
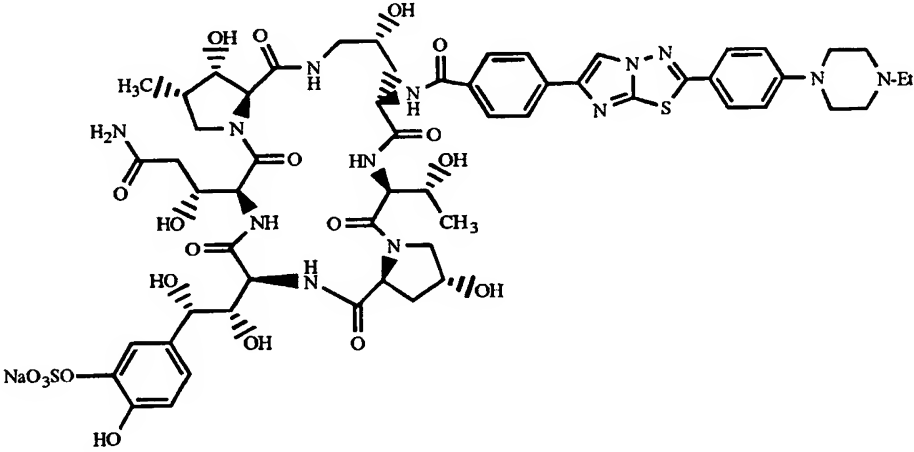
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfonatophenyl group. The molecule is composed of several interconnected rings and functional groups, including a sulfonate group (NaO<sub>3</sub>SO) and a hydroxyl group (HO) on a benzene ring.</p>
146	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-hydroxy-3-sulfonatophenyl group. The molecule is composed of several interconnected rings and functional groups, including a sulfonate group (NaO<sub>3</sub>SO) and a hydroxyl group (HO) on a benzene ring. The side chain is different from the one in the first structure, featuring a triazole ring system.</p>

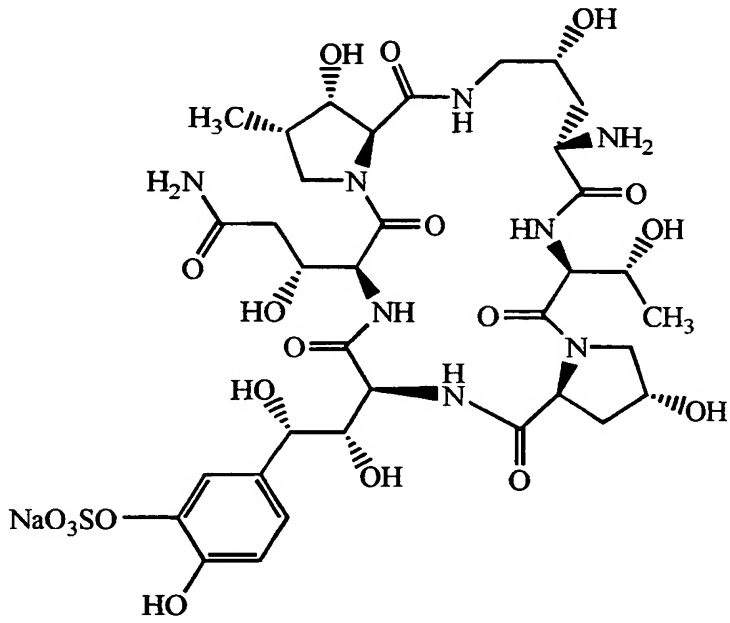
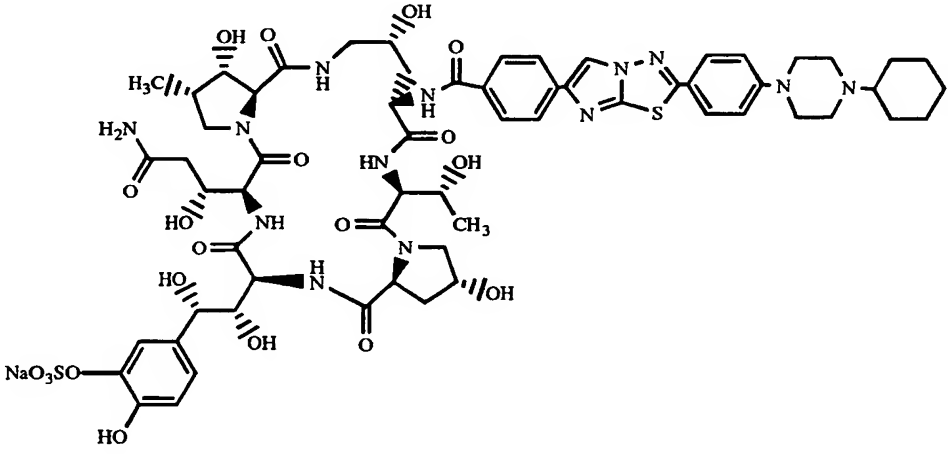
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 4-sulfamoylphenyl group. It features a central chain with various side groups including a methyl group, a hydroxyl group, and a sulfamoyl group.</p>
147	 <p>This structure is similar to the one above but features a different side chain, including a morpholine ring and a thiazole ring system.</p>

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. It features a central chain with various side groups, including a methyl group, a hydroxyl group, and a sulfonate group.</p>
148	 <p>This structure is similar to the one above but features a different side chain, including a thiazole ring and a morpholine derivative. It also contains a 3-hydroxy-4-sulfonatophenyl group and various stereocenters.</p>

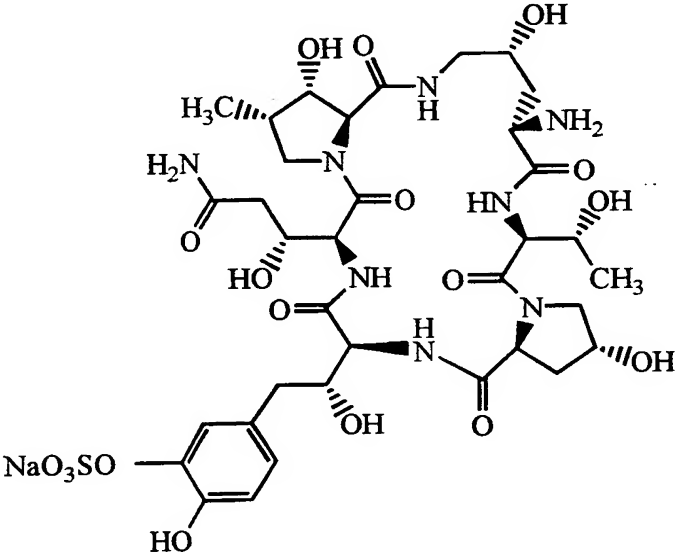
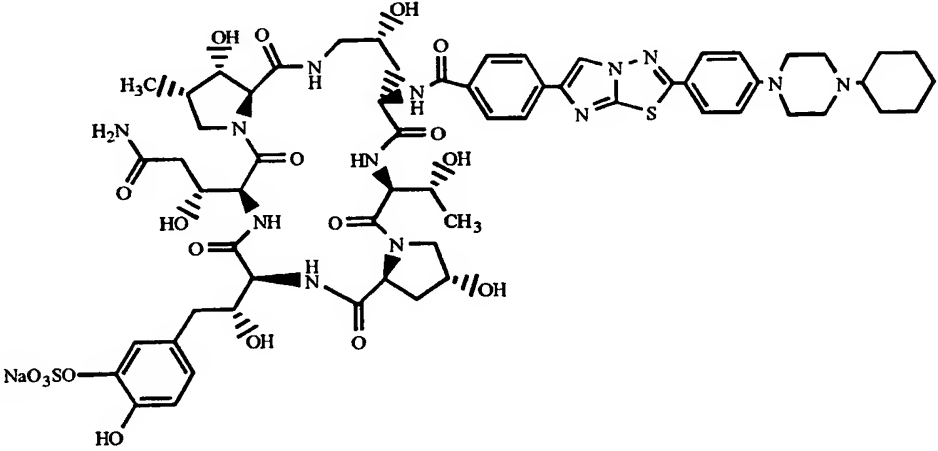
Example No.	Formula
149	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). Stereochemistry is indicated with wedges and dashes.</p>
	 <p>This structure is similar to the one above but features a different side chain, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). Stereochemistry is indicated with wedges and dashes.</p>

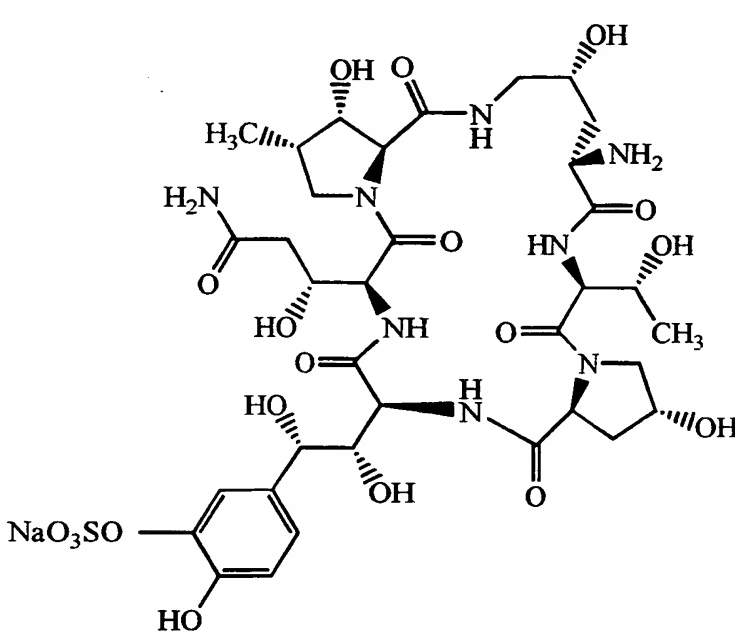
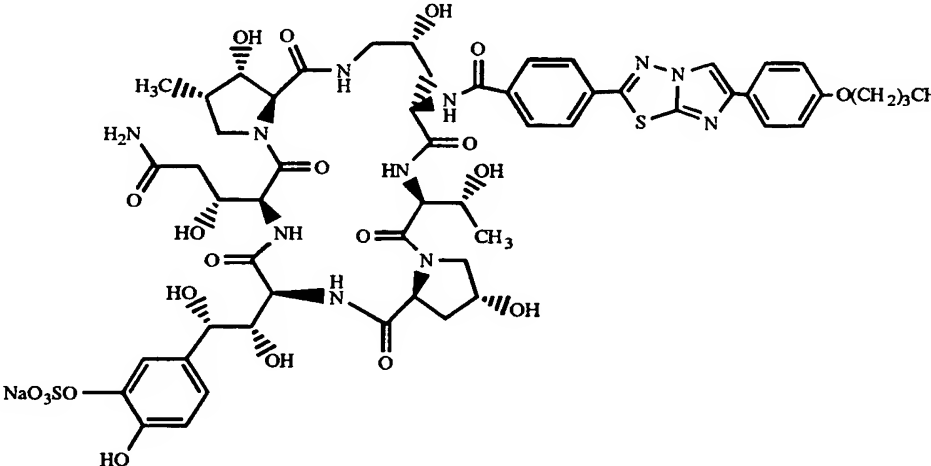
Example No.	Formula
	
150	

Example No.	Formula
	
151	

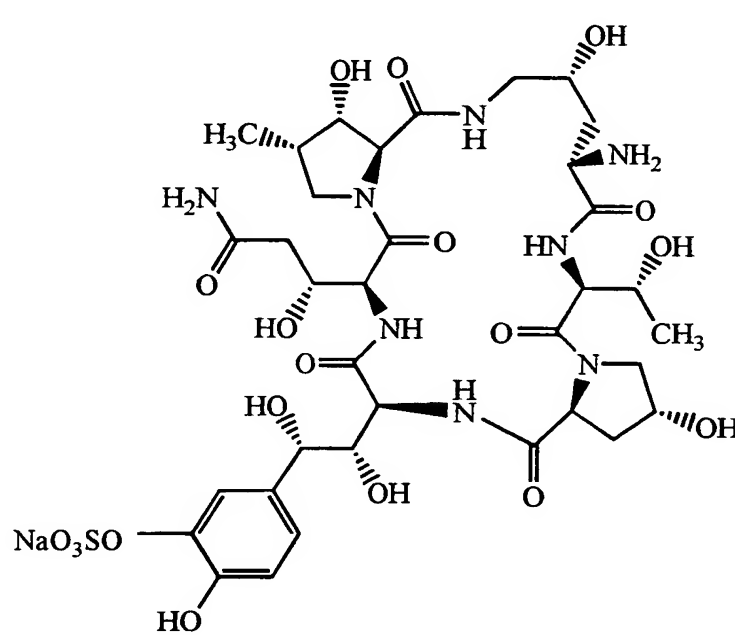
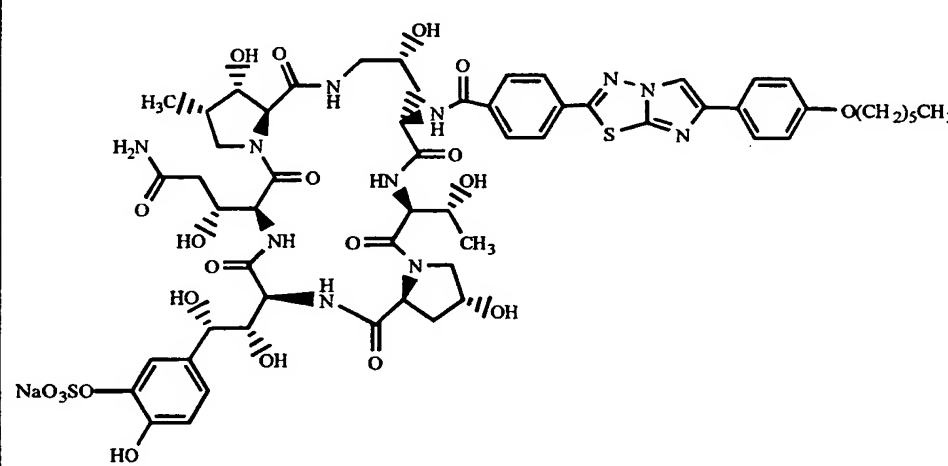
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. It features a central chain with various side groups, including a methyl group, a hydroxyl group, and a sulfonate group.</p>
152	 <p>The structure shows a complex molecule with multiple stereocenters, amide bonds, and a 3-hydroxy-4-sulfonatophenyl group. It features a central chain with various side groups, including a methyl group, a hydroxyl group, and a sulfonate group. The side chain is different from the one in the first structure, featuring a more complex aromatic system.</p>

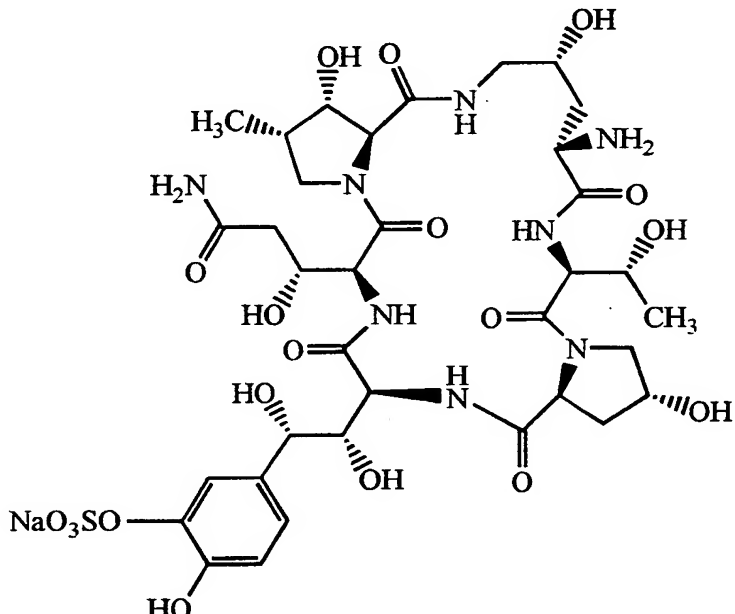
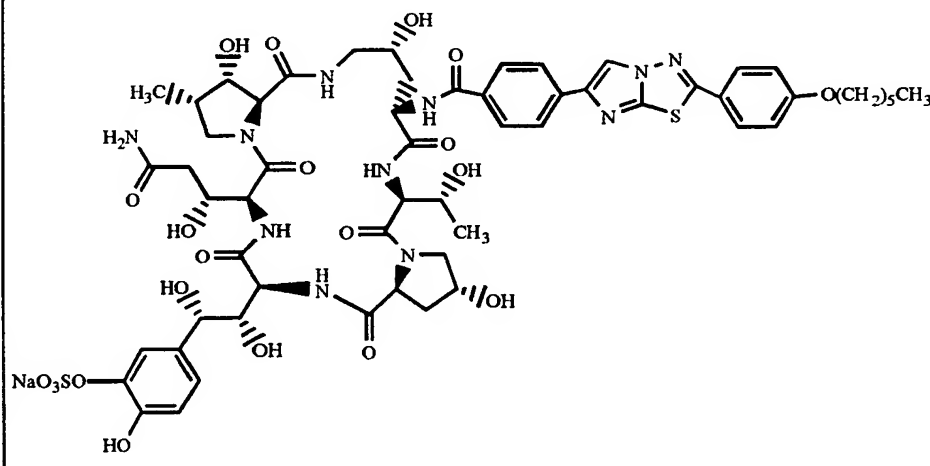


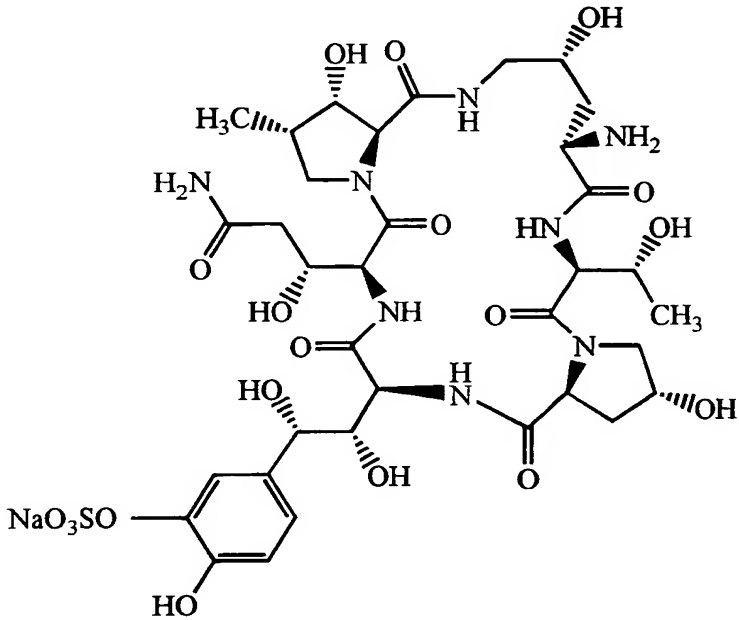
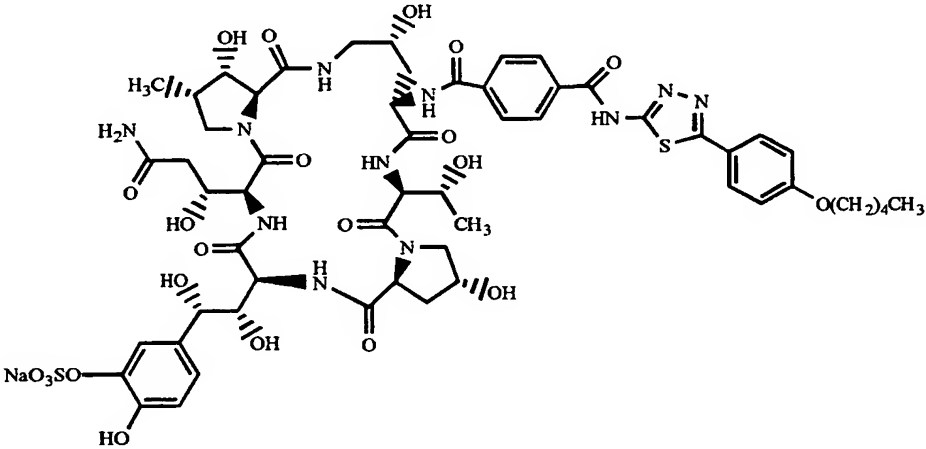
Example No.	Formula
	
153	

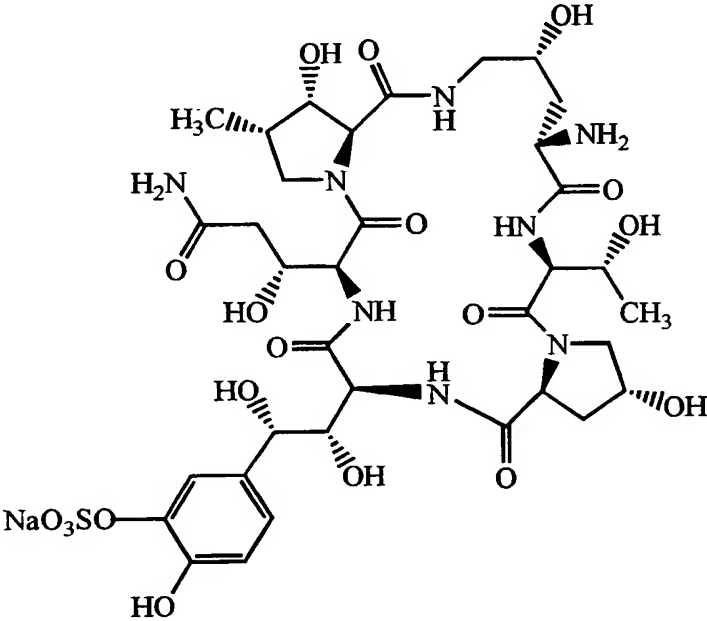
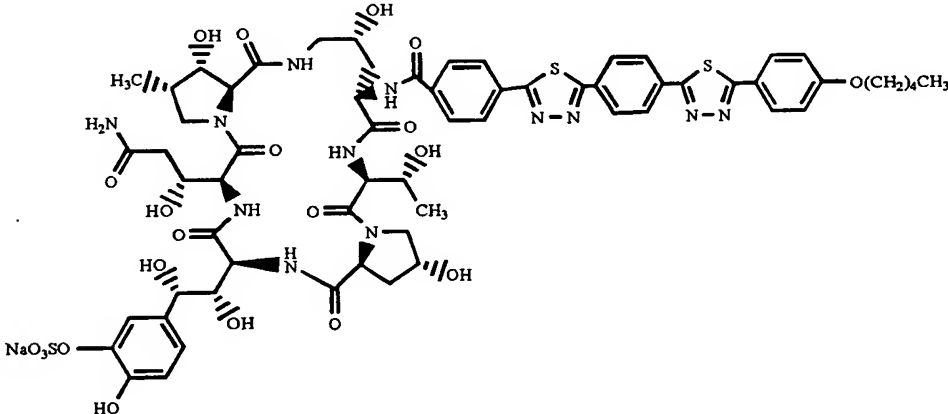
Example No.	Formula
154	 <p>The structure shows a complex molecule with multiple fused and linked rings. It includes a pyrazole ring, a thiazole ring, and a phenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO). The molecule is highly substituted with various functional groups, including hydroxyl groups, amide groups, and a methyl group.</p>
154	 <p>The structure shows a complex molecule with multiple fused and linked rings. It includes a pyrazole ring, a thiazole ring, and a phenyl group with a sodium sulfonate group (NaO<sub>3</sub>SO). The molecule is highly substituted with various functional groups, including hydroxyl groups, amide groups, and a methyl group.</p>

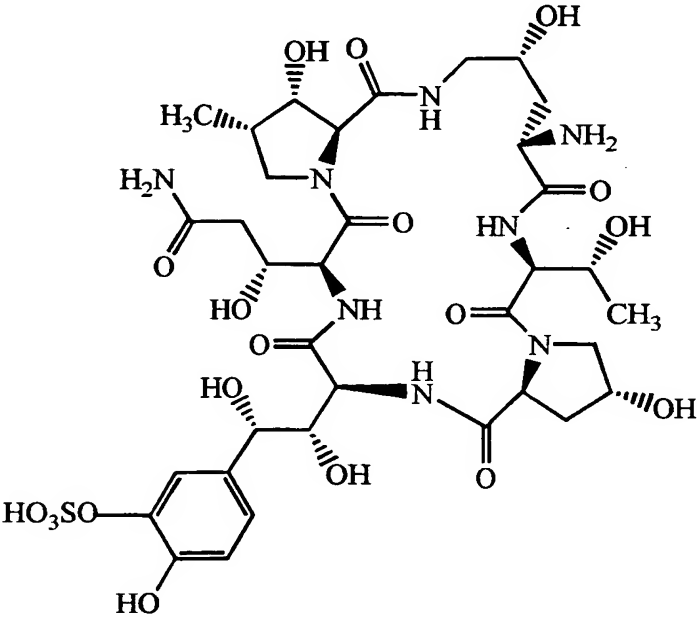
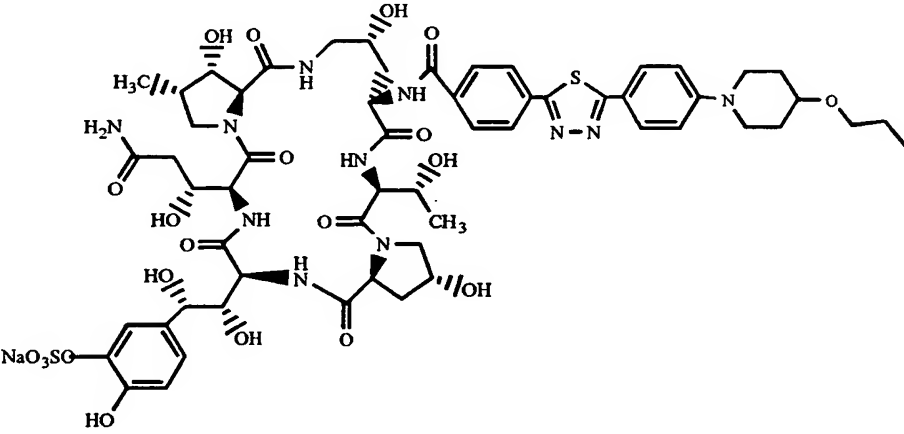
Example No.	Formula
155	

Example No.	Formula
	
156	

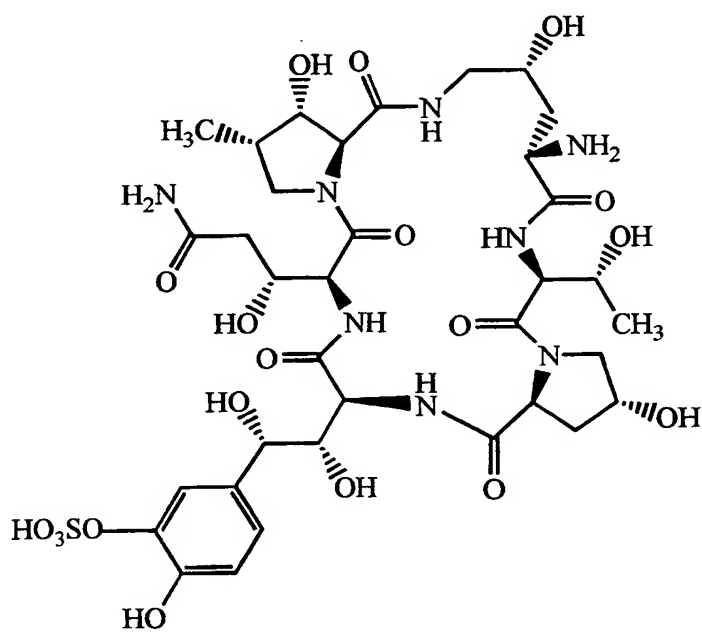
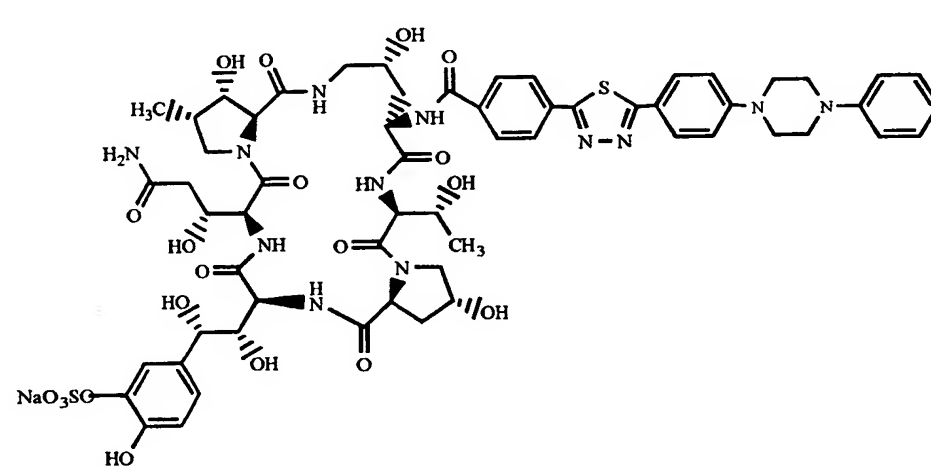
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple amide, ester, and hydroxyl groups. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-).</p>
157	 <p>The structure is similar to the one above, but with a different side chain. It features a central core with various side chains, including a sodium sulfonate group (NaO<sub>3</sub>SO-) and a hydroxyl group (HO-). The side chain includes a benzene ring with a hydroxyl group and a sodium sulfonate group, and a triethyl ether group (O(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub>).</p>

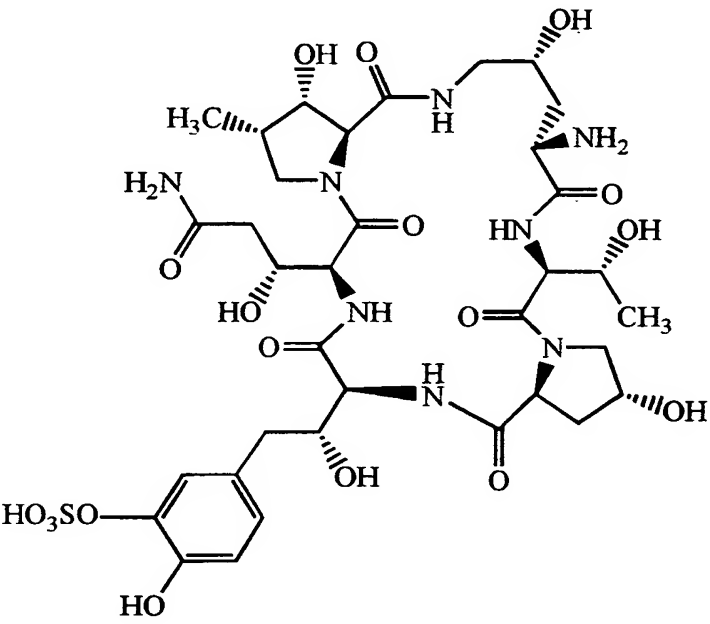
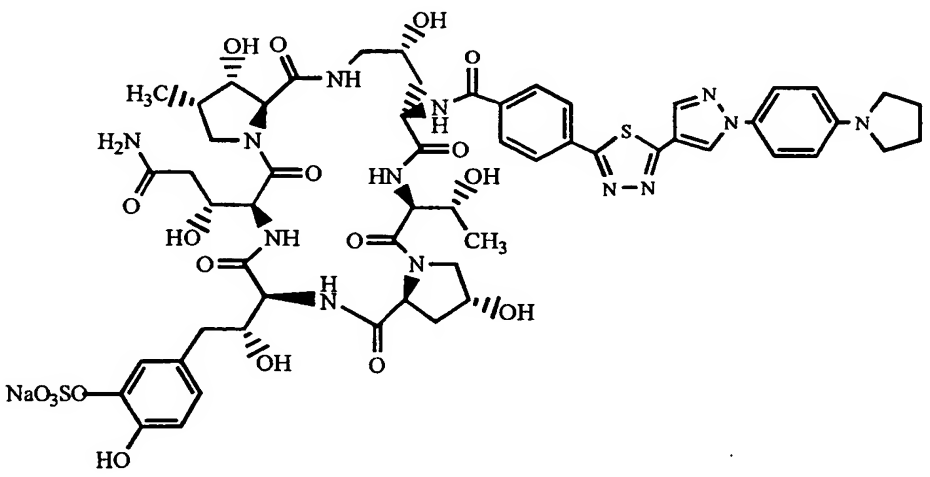
Example No.	Formula
	
158	

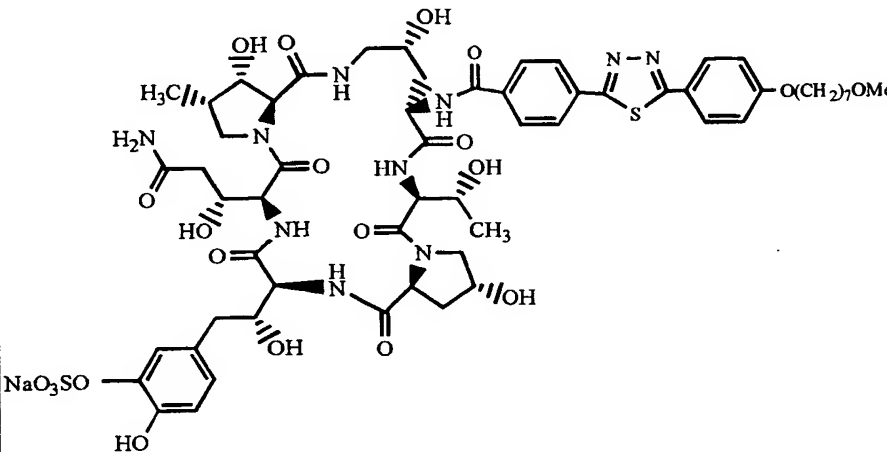
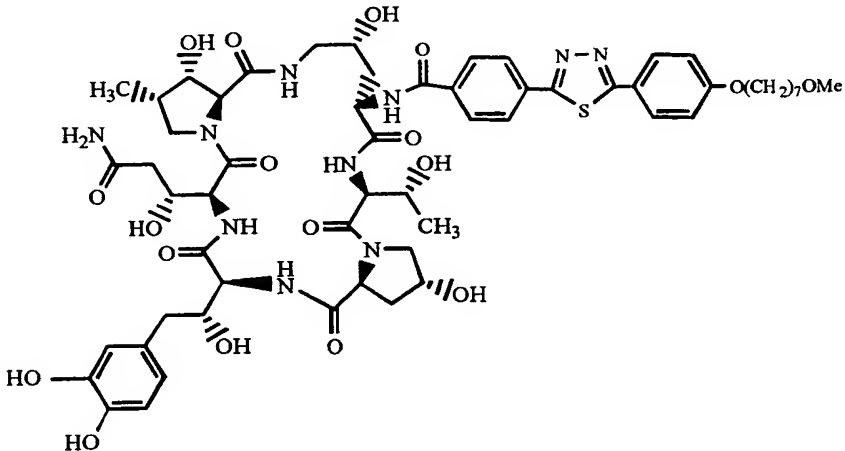
Example No.	Formula
159	
159	

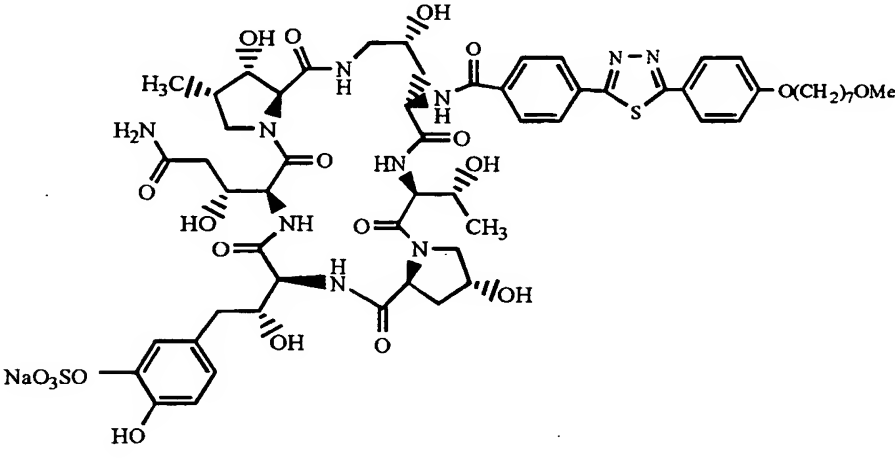
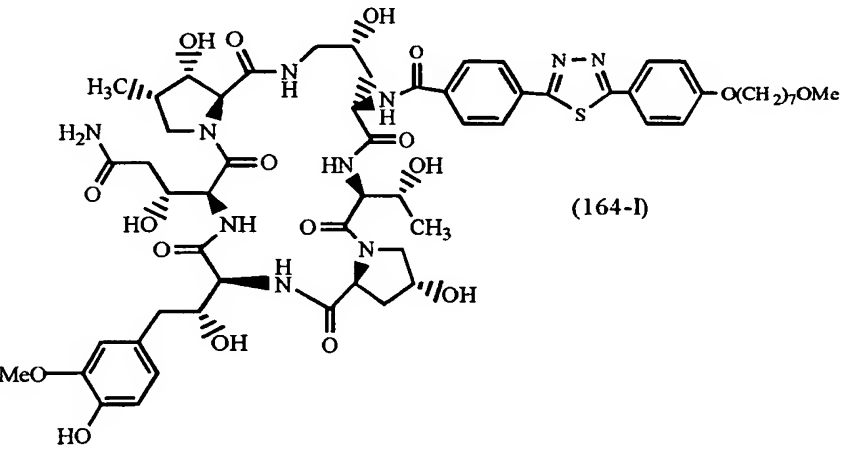
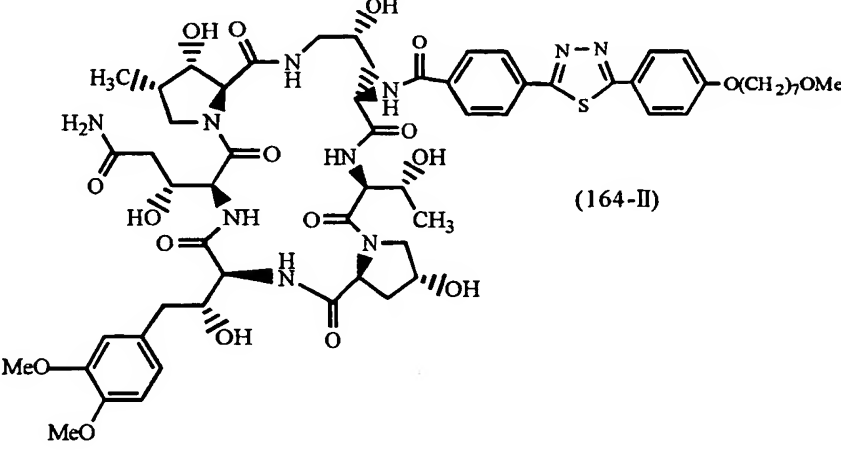
Example No.	Formula
	
160	

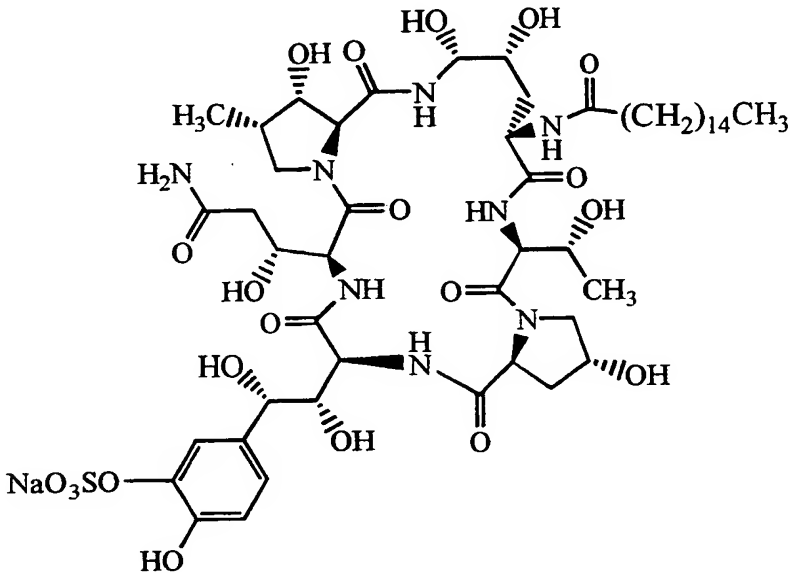
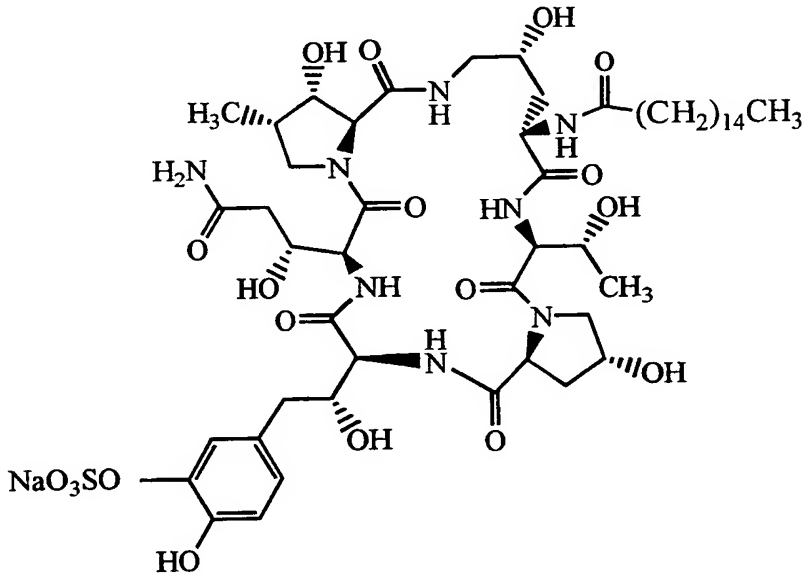


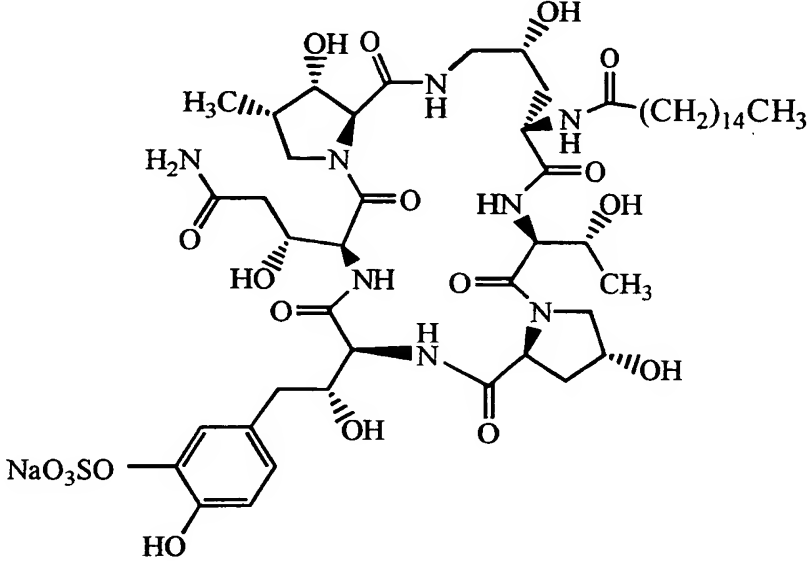
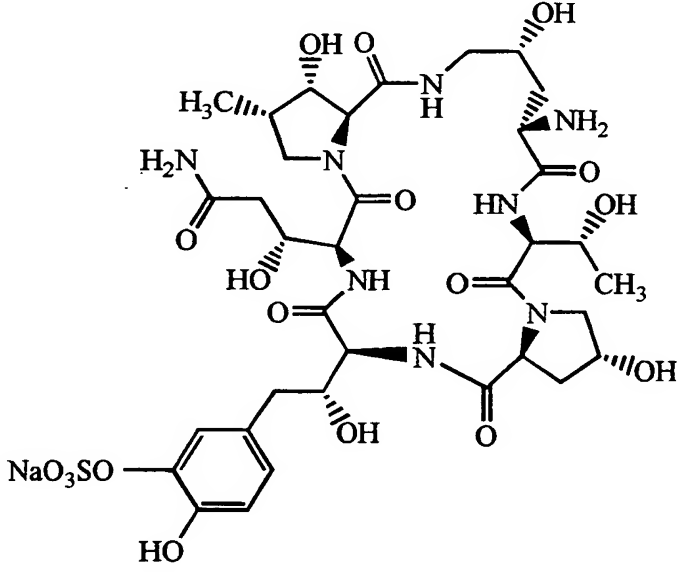
Example No.	Formula
	
161	

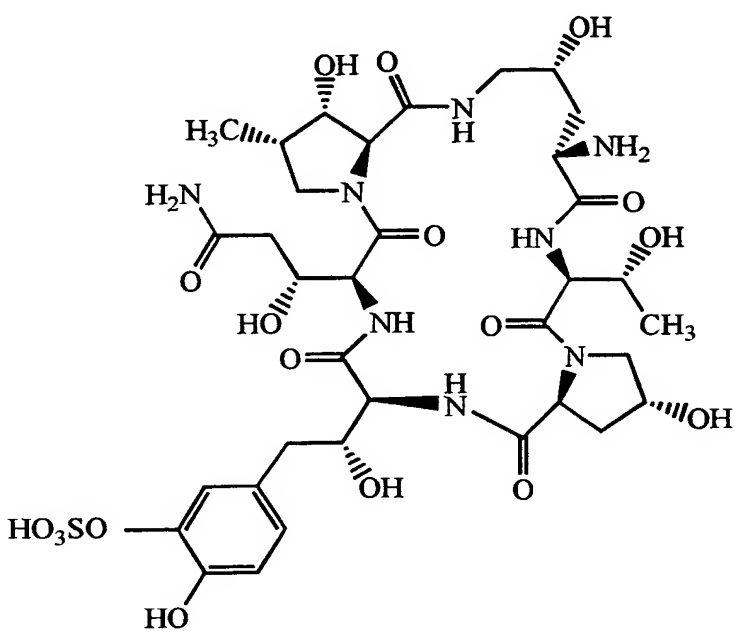
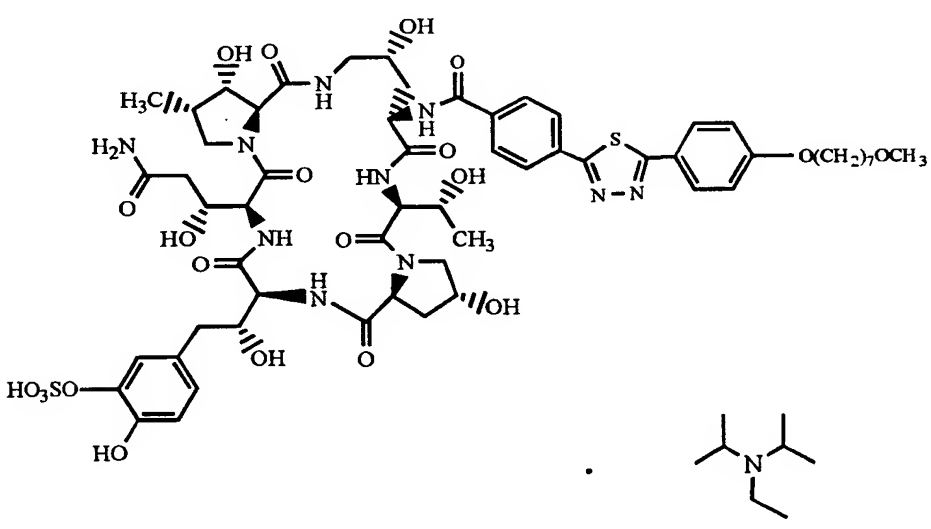
Example No.	Formula
	
162	

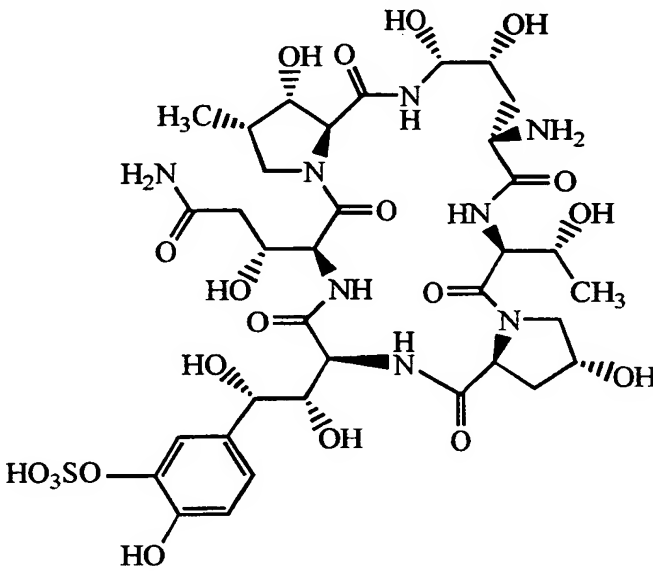
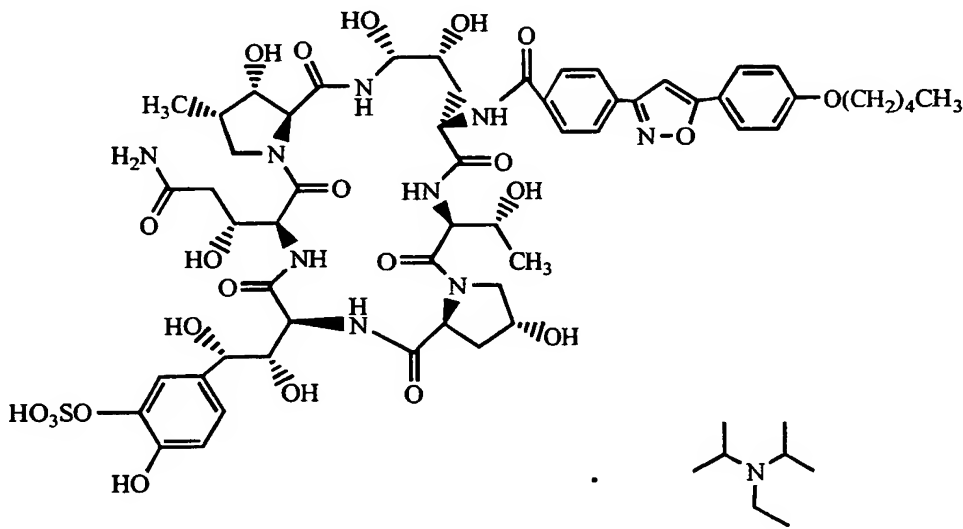
Example No.	Formula
	 <p>The structure shows a complex molecule with a central bicyclic core. It features multiple amide and ester groups, a long alkoxy chain (O(CH<sub>2</sub>)<sub>7</sub>OMe), and a sulfonate group (NaO<sub>3</sub>SO). Stereochemistry is indicated with wedges and dashes.</p>
163	 <p>The structure is identical to the one above, but the substituent on the phenyl ring is a hydroxyl group (HO) instead of a sulfonate group (NaO<sub>3</sub>SO).</p>

Example No.	Formula
164	 <p>Chemical structure of a complex molecule, likely a peptide derivative, featuring a central core with multiple hydroxyl groups, a methyl group, an amide group, and a sodium sulfonate group attached to a phenyl ring.</p>
	 <p>Chemical structure (164-I) of a complex molecule, similar to the one above, but with a methoxy group instead of a sodium sulfonate group.</p>
	 <p>Chemical structure (164-II) of a complex molecule, similar to the one above, but with two methoxy groups instead of a sodium sulfonate group.</p>

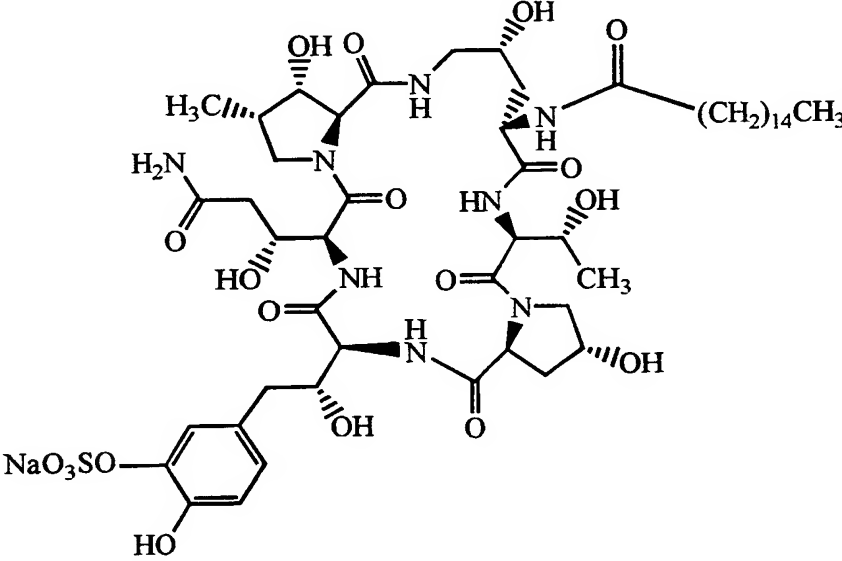
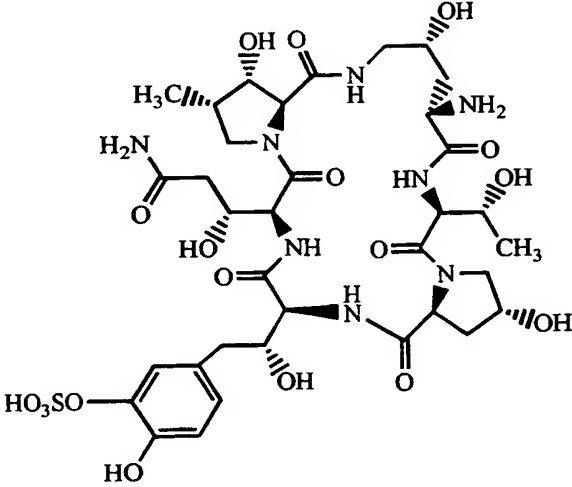
Example No.	Formula
	 <p>The structure shows a complex molecule with multiple fused and linked rings. It includes a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a long alkyl chain (CH<sub>2</sub>)<sub>14</sub>CH<sub>3</sub>. The molecule features several hydroxyl groups and amide linkages.</p>
165	 <p>This structure is similar to the one above but features a different linker between the sulfonate group and the main ring system. It includes a p-toluenesulfonate group (NaO<sub>3</sub>SO-) and a long alkyl chain (CH<sub>2</sub>)<sub>14</sub>CH<sub>3</sub>. The molecule features several hydroxyl groups and amide linkages.</p>

Example No.	Formula
	
166	

Example No.	Formula
	 <p>The structure shows a complex molecule with multiple fused and linked rings. It includes a p-toluenesulfonate group (HO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule features several amide bonds, hydroxyl groups, and a methyl group (H<sub>3</sub>C-).</p>
167	 <p>The structure shows a complex molecule with multiple fused and linked rings. It includes a p-toluenesulfonate group (HO<sub>3</sub>SO-) and a hydroxyl group (HO-). The molecule features several amide bonds, hydroxyl groups, a methyl group (CH<sub>3</sub>-), and a long alkoxy chain (O(CH<sub>2</sub>)<sub>7</sub>OCH<sub>3</sub>). A separate structure of a tertiary amine is also shown.</p>

Example No.	Formula
	
168	



Example No.	Formula
	
169	

Example 1

To a suspension of Starting Compound (1) (0.6 g) and sodium cyanoborohydride (0.076 g) in dichloromethane (6 ml) was gradually added trifluoroacetic acid (3 ml) at 4°C. The mixture was stirred for an hour at 4°C. The reaction mixture was evaporated under reduced pressure. The residue was added to water and adjusted to pH 8.5 with 1N NaOH aq. The solution was subjected to column chromatography on ODS (YMC-gel ODS-AM S-50) and eluted with 30% acetonitrile aqueous solution. The fractions containing the object compound were combined and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give Object Compound (1) (0.417 g).

IR (KBr) : 3350, 1668.1, 1629.6, 1241.9  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.2-1.55 (8H, m), 1.55-2.1 (5H, m), 2.1-2.5 (4H, m), 3.01 (1H, m), 3.19 (1H, m), 3.46 (1H, m), 3.6-3.87 (3H, m), 3.87-4.55 (13H, m), 4.6-5.5 (8H, m), 6.52 (1H, d,  $J=8.1\text{Hz}$ ), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.85 (1H, s), 7.0-7.15 (3H, m), 7.19 (1H, s), 7.27-7.55 (3H, m), 7.55-7.78 (3H, m), 7.8-8.0 (2H, m), 8.76 (1H, s), 8.85 (1H, s)

MASS (m/z) : 1248 ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{53}\text{H}_{72}\text{N}_9\text{NaO}_{21}\text{S}\cdot 7\text{H}_2\text{O}$  :

C 47.07, H 6.41, N 9.32

Found : C 46.82, H 6.54, N 9.25

The following compounds (Examples 2 and 3) were obtained in a manner similar to that of Example 1.

Example 2

IR (KBr) : 3349.7, 1666.2, 1631.5, 1267.0  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.9\text{Hz}$ ), 1.7-2.0 (2H, m), 2.0-2.6 (4H, m), 2.6-2.8 (1H, m), 3.1-3.3 (1H, m), 3.3-3.5 (1H, m), 3.5-4.5 (16H, m), 4.6-4.9 (2H, m), 5.1-5.5 (5H, m), 6.72 (1H, d,  $J=8.2\text{Hz}$ ), 6.81 (1H, dd,  $J=8.2$  and  $1.9\text{Hz}$ ),

387

6.9-7.5 (4H, m), 7.05 (1H, d, J=1.9Hz), 7.4-7.9 (3H, m), 8.84 (1H, s)

MASS (m/z) : 965 (M+Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>35</sub>H<sub>51</sub>N<sub>8</sub>O<sub>19</sub>SNa·5.5H<sub>2</sub>O :

5 C 40.35, H 6.00, N 10.75

Found : C 40.33, H 5.92, N 10.63

Example 3

IR (KBr) : 3350, 1648.8, 1276.6 cm<sup>-1</sup>

MASS (m/z) : 1266 (M-Na<sup>+</sup>)

10 Example 4

To a suspension of Starting Compound (4) (46.1 g) and NaBH<sub>3</sub>CN (7.7 g) in dichloromethane (600 ml) was added dropwise trifluoroacetic acid (240 ml) for 15 minutes below 5°C. The reaction mixture was stirred for 3 hours at the same temperature.  
15 The lower layer (trifluoroacetic acid layer) of the reaction mixture was poured into a large volume of an ice cooled aqueous NaHCO<sub>3</sub> solution (pH=8.5). The upper layer (dichloromethane layer) was also poured into a large volume of an ice cooled aqueous NaHCO<sub>3</sub> solution. The aqueous layer was combined together and  
20 was purified by column chromatography on ODS to afford Object Compound (4).

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.7Hz), 1.04-1.12 (3H, m), 1.48-2.00 (3H, m), 2.07-2.50 (4H, m), 2.90-3.34 (2H, m), 3.60-4.48 (18H, m), 4.60-5.40 (9H, m), 6.72 (1H, d, J=8.2Hz), 6.81 (1H, dd, J=8.2 and 1.6Hz), 6.84 (1H, m), 6.98 (1H, m), 7.04 (1H, d, J=1.6Hz), 7.28-7.50 (6H, m), 7.58 (2H, m), 7.73 (2H, d, J=7.4Hz), 7.84 (1H, m), 7.88 (2H, d, J=7.6Hz), 8.84 (1H, s)

30 MASS (m/z) : 1141 (M<sup>+</sup>)

Example 5

To a solution of Starting Compound (5) (38.7 g) in dimethylformamide (250 ml) was added piperidine (17 ml) at room temperature. The solution was stirred for 2.5 hours at the same  
35 temperature. Ethyl acetate (2.5 L) was added to the reaction

mixture and the mixture was stirred for 30 minutes. The powder was collected by filtration to give Object Compound (5) (34.6 g).

#### Example 6

5 To a solution of Starting Compound (6) (0.3 g) and triethylsilane (0.44 ml) in methylene chloride (7 ml) at 10°C, was added dropwise trifluoroacetic acid (2 ml). The mixture was stirred at room temperature for 4 hours. The reaction mixture was added in 1N-sodium hydroxide (31 ml) at 10°C. The aqueous  
10 layer was subjected to column chromatography on ODS (YMC-gel ODS-AM S-50 (Trademark: prepared by Yamamura Chemical Lab.)) eluting with water. The fractions containing the object compound were combined, and evaporated under reduced pressure. The residue was lyophilized to give Object Compound (6) (0.13  
15 g).

IR (KBr) : 3361.3, 1668.1, 1631.5, 1268.9  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.06 (3H, d,  $J=5.5\text{Hz}$ ), 1.60-2.50 (9H, m), 2.90-2.97 (1H, m),  
20 3.16-3.50 (2H, m), 3.69-4.50 (13H, m), 4.74-5.31 (10H, m), 6.72-7.65 (14H, m), 7.93-7.97 (1H, m), 8.71 (1H, s)

#### Example 7

To a solution of Starting Compound (7) (110 mg) in water (5 ml) was added 10% palladium on carbon (11 mg), and hydrogen  
25 gas at atmosphere pressure for 7 hours. The reaction mixture was filtered through celite and lyophilized to give Object Compound (7) (70 mg).

IR (KBr) : 3394, 3327, 1676, 1633, 1439  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.8\text{Hz}$ ), 1.08 (3H, d,  $J=6.0\text{Hz}$ ), 1.88-5.83 (35H, m), 6.68-8.71 (10H, m)

MASS (m/z) : 903.17 ( $M-\text{Na}^+$ )

#### Example 8

To a solution of Starting Compound (8) (350 mg) in N,N-dimethylformamide (6 ml) was added 4-[4-(4-cyclohexylphenyl)-  
35 piperazin-1-yl]benzoic acid benzotriazol-1-yl ester (230 mg),

and the mixture was stirred for 2 hours at ambient temperature. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and dried under reduced pressure. The powder was dissolved in water, and subjected to  
5 column chromatography on ion exchange resin (DOWEX-50WX4 (Trademark: prepared by Dow Chemical)) eluting with water. The fractions containing the object compound were combined, and subjected to column chromatography on ODS (YMC-gel·ODS-AM·S-50 (Trademark: prepared by Yamamura Chemical Lab.)) eluting with  
10 30% acetonitrile in water. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give Object Compound (8) (160 mg).

15 IR (KBr) : 1666.2, 1633.4, 1608.3, 1511.9, 1230.4  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.09 (3H, d,  $J=5.4\text{Hz}$ ), 1.2-1.5 (6H, m), 1.6-2.1 (7H, m), 2.1-2.6 (5H, m), 3.02 (1H, m), 3.1-3.5 (10H, m), 3.6-4.5 (14H, m), 4.6-5.3 (9H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.77 (1H, d,  $J=8.2\text{Hz}$ ), 6.80 (1H, s), 6.91 (2H, d,  $J=8.7\text{Hz}$ ),  
20 6.9-7.1 (5H, m), 7.26 (1H, s), 7.3-7.5 (2H, m), 7.66 (1H, br s), 7.78 (2H, d,  $J=8.6\text{Hz}$ ), 8.04 (1H, d,  $J=7.3\text{Hz}$ ), 8.31 (1H, d,  $J=7.3\text{Hz}$ ), 8.84 (1H, s)

MASS (m/z) : 1311 ( $\text{M}+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{77}\text{N}_{10}\text{O}_{20}\text{S}\cdot 6\text{H}_2\text{O}$  :

25 C 49.85, H 6.42, N 10.02  
Found : C 50.06, H 6.36, N 10.07

The following compounds (Examples 9 to 11) were obtained in a manner similar to that of Example 8.

Example 9

30 IR (KBr) : 3350, 1648.8, 1276.6  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.8\text{Hz}$ ), 1.11 (3H, d,  $J=5.2\text{Hz}$ ), 1.5-1.7 (6H, m), 1.7-2.6 (7H, m), 2.94 (1H, m), 3.1-3.5 (6H, m), 3.6-4.6 (14H, m), 4.7-5.3 (9H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.82 (1H, d,  $J=8.2\text{Hz}$ ), 6.84  
35 (1H, s), 7.04 (1H, s), 7.06 (2H, d,  $J=8.7\text{Hz}$ ), 7.18 (1H,

390

s), 7.3-7.5 (2H, m), 7.66 (1H, br s), 7.83 (2H, d, J=8.7Hz), 8.0-8.2 (5H, m), 8.75 (1H, d, J=7.1Hz), 8.84 (1H, s)

MASS (m/z) : 1266 (M-Na<sup>+</sup>)

5 Example 10

IR (KBr) : 3361.3, 1646.9, 1517.7, 1257.4 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=7.3Hz), 0.96 (3H, d, J=6.5Hz), 1.11 (3H, d, J=5.7Hz), 1.3-1.6 (4H, m), 1.6-2.6 (9H, m), 2.95 (1H, m), 3.1-3.5 (2H, m), 3.6-4.6 (16H, m), 4.7-5.4 (9H, m), 6.73 (1H, d, J=8.2Hz), 6.82 (1H, d, J=8.2Hz), 6.90 (1H, s), 7.06 (1H, s), 7.14 (2H, d, J=8.9Hz), 7.23 (1H, s), 7.3-7.5 (2H, m), 7.68 (1H, br s), 7.90 (2H, d, J=8.9Hz), 7.8-8.2 (5H, m), 8.60 (1H, d, J=6.7Hz), 8.85 (2H, s)

15 MASS (m/z) : 1308 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>57</sub>H<sub>70</sub>N<sub>11</sub>O<sub>21</sub>S<sub>2</sub>Na·10H<sub>2</sub>O :

C 45.26, H 6.00, N 10.19

Found : C 45.05, H 5.83, N 10.19

Example 11

20 NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.7Hz), 1.12 (3H, d, J=6.0Hz), 1.2-1.6 (8H, m), 1.6-2.6 (9H, m), 2.9-3.1 (1H, m), 3.1-3.5 (7H, m), 3.6-4.6 (16H, m), 4.6-5.4 (9H, m), 6.74 (1H, d, J=8.2Hz), 6.83 (1H, d, J=8.2Hz), 6.89 (1H, s), 7.05 (1H, s), 7.13 (2H, d, J=8.8Hz), 7.16 (1H, m), 7.3-7.6 (2H, m), 7.67 (1H, br), 7.97 (2H, d, J=8.8Hz), 7.9-8.2 (5H, m), 8.7-9.0 (2H, m)

25 MASS (m/z) : 1327.07 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>58</sub>H<sub>75</sub>N<sub>10</sub>NaO<sub>22</sub>S<sub>2</sub>·5H<sub>2</sub>O :

C 48.33, H 5.94, N 9.72

30 Found : C 48.27, H 6.05, N 9.69

Example 12

To a solution of Starting Compound (12) (60.0 g) and diethylisopropylamine (16.6 ml) in diethylformamide (340 ml) was added 4-[5-[4-(6-methoxy-n-hexyloxy)phenyl]-1,3,4-

thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester (37.4 g) at room temperature. The solution was stirred for 17 hours at the same temperature. Ethyl acetate (3.4 L) was added to the reaction mixture and the mixture was stirred for 30 minutes. The powder was collected by filtration and washed with ethyl acetate (3.5 L) to give crude N-acylated Starting Compound (12) (93.0 g). This material was used without further purification. To a suspension of crude N-acylated Starting Compound (12) (93.0 g) and  $\text{NaBH}_3\text{CN}$  (9.0 g) in dichloromethane (900 ml), was added trifluoroacetic acid (450 ml) at  $0^\circ\text{C}$  over 30 minutes. The solution was stirred for 2 hours at the same temperature. The reaction mixture was slowly poured into an ice cooled aqueous NaOH solution ( $8 < \text{pH} < 11$ , Temperature  $< 7^\circ\text{C}$ ). The separated organic layer was extracted with water twice. The combined aqueous solution was subjected to column chromatography on SP20 (7 L), washing with water, and eluting with 60% aqueous  $\text{CH}_3\text{CN}$ . The eluent was concentrated to remove  $\text{CH}_3\text{CN}$  and chromatographed by reverse-phase (ODS) flash chromatography eluting with 17%  $\text{CH}_3\text{CN}$ /water, followed by lyophilization of the appropriate fractions to provide 28.3 g of Object Compound (12).

NMR ( $\text{DMSO}-d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.12 (3H, d,  $J=5.9\text{Hz}$ ), 1.30-1.60 (6H, m), 1.65-2.60 (9H, m), 2.80-3.50 (5H, m), 3.22 (3H, s), 3.60-4.60 (14H, m), 4.07 (2H, t,  $J=6.7\text{Hz}$ ), 4.60-5.30 (9H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.89 (1H, s), 7.05 (1H, s), 7.13 (2H, d,  $J=8.9\text{Hz}$ ), 7.16 (1H, s), 7.42-7.46 (2H, m), 7.66 (1H, br), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 8.07-8.13 (5H, m), 8.77 (1H, d,  $J=6.8\text{Hz}$ ), 8.84 (1H, s)

MASS ( $m/z$ ) : 1313.25 ( $\text{M}-\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{57}\text{H}_{73}\text{N}_{10}\text{O}_{22}\text{S}_2\text{Na}\cdot 7\text{H}_2\text{O}$  :

C 46.78, H 5.99, N 9.57

Found : C 46.56, H 5.94, N 9.45

### Example 13

A solution of Starting Compound (13) (400 mg) in N,N-

392

dimethylformamide (4 ml) was treated with 4-[5-[4-(6-methoxy-n-hexyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotriazol-1-yl ester (343 mg) then stirred 15 hours at room temperature. Ethyl acetate was added to the reaction mixture and the resulting precipitate were collected by filtration, washed thoroughly with ethyl acetate and dried. The powder was dissolved in saturated sodium hydrogen carbonate solution, filtered then purified by ODS column chromatography (YMC-gel ODS-AM S-50) eluting with 19-21% aqueous acetonitrile. Product-containing fractions were pooled, evaporated to remove acetonitrile, and lyophilized to give Object Compound (13) (306.4 mg) as an amorphous white powder.

IR (KBr) : 1675.8, 1650.8, 1631.5, 1540.8, 1513.8,  
1452.1, 1257.4  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.09 (3H, d,  $J=5.4\text{Hz}$ ), 1.30-1.60 (6H, m), 1.65-2.60 (10H, m), 2.80-4.60 (17H, m), 3.22 (3H, s), 3.32 (2H, t,  $J=6.3\text{Hz}$ ), 4.07 (2H, t,  $J=6.5\text{Hz}$ ), 4.68-5.80 (8H, m), 6.68 (1H, d,  $J=8\text{Hz}$ ), 6.76 (1H, d,  $J=8\text{Hz}$ ), 6.86 (1H, s), 6.98 (1H, s), 7.13 (2H, d,  $J=8.8\text{Hz}$ ), 7.16 (1H, s), 7.30-7.50 (3H, m), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 8.03-8.13 (4H, m), 8.76-8.79 (2H, m)

MASS ( $m/z$ ) : 1343.13 ( $M+\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{57}\text{H}_{73}\text{N}_{10}\text{O}_{21}\text{S}_2\text{Na}\cdot 8\text{H}_2\text{O}$  :

C 46.72, H 6.12, N 9.56

Found : C 46.66, H 5.97, N 9.53

The following compound was obtained in a manner similar to that of Example 13.

#### Example 14

IR (KBr) : 1675.8, 1650.8, 1631.5, 1540.8, 1513.8,  
1450.2  $\text{cm}^{-1}$

NMR ( $\text{DMSO-d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.10 (3H, d,  $J=5.9\text{Hz}$ ), 1.12-1.80 (8H, m), 1.80-2.60 (10H, m), 2.90-3.05 (1H, m), 3.21 (3H, s), 3.27 (2H, t,  $J=6.3\text{Hz}$ ), 3.30-3.50 (2H, m), 3.68-4.60 (14H, m), 4.07 (2H, t,



393

J=6Hz), 4.70-5.45 (8H, m), 6.71 (1H, d, J=8.2Hz), 6.79 (1H, d, J=8.2Hz), 6.87 (1H, s), 6.97 (1H, s), 7.13 (2H, d, J=8.9Hz), 7.15 (1H, s), 7.42-7.71 (3H, m), 7.97 (2H, d, J=8.7Hz), 8.03-8.12 (4H, m), 8.73-8.81 (3H, m)

5      MASS (m/z) : 1311.32 (M-Na<sup>+</sup>)  
       Elemental Analysis Calcd. for C<sub>58</sub>H<sub>75</sub>N<sub>10</sub>O<sub>21</sub>S<sub>2</sub>Na·7H<sub>2</sub>O :  
                                         C 47.67, H 6.14, N 9.58  
                  Found :     C 47.49, H 6.09, N 9.47

### Example 15

10 A solution of Starting Compound (15) (508 mg) in  
N,N-dimethylformamide (10 ml) was treated with 4-[5-[4-(6-  
methoxy-n-hexyloxy)phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid  
benzotriazol-1-yl ester (428 mg) and the mixture was stirred 18  
15 hours at room temperature. Ethyl acetate was added to the  
reaction mixture and the resulting precipitate was collected by  
filtration, washed thoroughly with ethyl acetate and dried. The  
powder was dissolved in saturated sodium hydrogen carbonate  
solution (100 ml), treated with water (100 ml), then purified  
by ODS column chromatography (YMC-gel ODS-AM S-50) eluting with  
20 16-17% aqueous acetonitrile. Fractions containing the object  
compound were combined, evaporated to remove acetonitrile, and  
lyophilized to give Object Compound (15) (400 mg) as an amorphous  
white powder.

IR (KBr) : 1668.1, 1650.8, 1631.5, 1538.9, 1513.8,  
1450.2, 1259.3  $\text{cm}^{-1}$

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.12 (3H, d, J=5.9Hz), 1.30-1.60 (6H, m), 1.65-2.60 (9H, m), 2.80-3.50 (5H, m), 3.22 (3H, s), 3.60-4.60 (14H, m), 4.07 (2H, t, J=6.7Hz), 4.60-5.30 (9H, m), 6.73 (1H, d, J=8.2Hz), 6.83 (1H, d, J=8.2Hz), 6.89 (1H, s), 7.05 (1H, s), 7.13 (2H, d, J=8.9Hz), 7.16 (1H, s), 7.42-7.46 (2H, m), 7.66 (1H, br), 7.97 (2H, d, J=8.8Hz), 8.07-8.13 (5H, m), 8.77 (1H, d, J=6.8Hz), 8.84 (1H, s)

35            MASS (m/z) : 1313.25 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for  $C_{57}H_{73}N_{10}O_{22}S_2Na \cdot 7H_2O$  :

C 46.78, H 5.99, N 9.57

Found : C 46.56, H 5.94, N 9.45

#### Example 16

5 To a solution of Starting Compound (16) (200 mg) and  
4-[5-(4-piperidin-1-yl-phenyl)-1,3,4-thiadiazol-2-yl]benzoic  
acid benzotriazol-1-yl ester in N,N-dimethylformamide (3 ml) was  
added dimethylaminopyridine (0.034 g), and the mixture was  
stirred for 6.5 hours at ambient temperature. The reaction  
10 mixture was pulverized with ethyl acetate. The precipitate was  
collected by filtration, and dried under reduced pressure. The  
solid was dissolved in water, and subjected to column  
chromatography on ion exchange resin (DOWEX-50WX4 (Trademark:  
prepared by Dow Chemical)) eluting with water. The fractions  
15 containing the object compound were combined, and subjected to  
column chromatography on ODS (YMC-gel ODS-AM S-50 (Trademark:  
prepared by Yamamura Chemical Lab.)) eluting with 50% methyl  
alcohol aqueous solution. The fractions containing the object  
compound were combined, and evaporated under reduced pressure  
20 to remove methanol. The residue was lyophilized to give Object  
Compound (16) (190 mg).

IR (KBr) : 3367, 1651, 1539, 1443  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95-5.30 (49H, m), 6.63-8.72 (19H, m)

MASS (m/z) : 1250.22 (M- $Na^+$ )

25 Elemental Analysis Calcd. for  $C_{55}H_{68}N_{11}NaO_{19}S_2 \cdot 12H_2O$  :

C 44.05, H 6.25, N 10.27

Found : C 43.94, H 5.76, N 10.14

#### Example 17

To a solution of 1-hydroxybenzotriazole (64 mg) and  
30 4-[2-(4-butyloxyphenyl)imidazo[2,1-b][1,3,4]thiadiazol-6-yl]  
benzoic acid (125 mg) in N,N-dimethylformamide (4 ml) was added  
1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride  
(73 mg) and the mixture was stirred for 4 hours at ambient  
temperature. Then to the reaction mixture was added Starting  
35 Compound (17) (200 mg) and the mixture was stirred for 4 hours

at ambient temperature. The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration and dried over reduced pressure. The powder was added to saturated sodium bicarbonate aqueous solution and subjected to column chromatography on ODS (YMC-gel ODS-AM S-50) and eluted with 30% acetonitrile in water. The fractions containing the object compound were combined and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give Object Compound (17) (123 mg).

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=7.3\text{Hz}$ ), 0.96 (3H, d,  $J=7.2\text{Hz}$ ), 1.11 (3H, d,  $J=5.5\text{Hz}$ ), 1.3-1.6 (2H, m), 1.6-2.6 (9H, m), 2.95 (1H, m), 3.1-3.5 (2H, m), 3.6-4.6 (16H, m), 4.7-5.5 (9H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.82 (1H, d,  $J=8.2\text{Hz}$ ), 6.89 (1H, s), 7.05 (1H, s), 7.14 (2H, d,  $J=8.9\text{Hz}$ ), 7.24 (1H, s), 7.3-7.5 (2H, m), 7.68 (1H, br s), 7.90 (2H, d,  $J=8.9\text{Hz}$ ), 7.8-8.1 (5H, m), 8.56 (1H, d,  $J=6.7\text{Hz}$ ), 8.85 (2H, s)

15 MASS (m/z) : 1341 ( $M+Na^+$ )

#### Example 18

20 To a suspension of Starting Compound (18) (1.70 g) and triethylsilane (1.58 g) in dichloromethane (15 ml) was added trifluoroacetic acid (15 ml) dropwise, and the mixture was stirred for 30 minutes under nitrogen atmosphere. The reaction mixture was evaporated under reduced pressure. The residue was dissolved in pH 6.86 phosphate-buffer, and adjusted to pH 9.5 with 1N sodium hydroxide aqueous solution. The solution was subjected to column-chromatography on ODS (YMC-gel ODS-AM S-50) and eluted with 30% acetonitrile aqueous solution (v/v). The fractions containing the object compound were combined and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give Object Compound (18) (136 mg).

25 IR (KBr) : 3350, 2933, 1668, 1635, 1540, 1471, 1249, 1045  $\text{cm}^{-1}$

30 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.6 (8H, m),

396

1.6-2.4 (10H, m), 2.8-4.1 (16H, m), 4.1-5.3 (11H, m),  
6.6-7.2 (9H, m), 7.3-7.7 (3H, m), 7.9-8.3 (4H, m),  
8.7-8.9 (1H, d, J=6.0Hz), 9.04 (1H, s)

MASS (m/z) : 1244.5 (M+Na<sup>+</sup>)5 Elemental Analysis Calcd. for C<sub>54</sub>H<sub>72</sub>N<sub>9</sub>O<sub>20</sub>NaS·6H<sub>2</sub>O :

C 48.75, H 6.36, N 9.48

Found : C 48.53, H 6.24, N 9.40

The following compounds [Examples 19 and 20] were obtained  
in a manner similar to that of Example 18.

10 Example 19

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, t, J=7.3Hz), 0.96 (3H, d,  
J=7.1Hz), 1.10 (3H, d, J=5.8Hz), 1.3-1.6 (2H, m),  
1.6-2.6 (10H, m), 2.95 (1H, m), 3.1-3.5 (2H, m),  
3.6-4.6 (16H, m), 4.7-5.4 (8H, m), 6.71 (1H, d,  
15 J=8.1Hz), 6.78 (1H, d, J=8.1Hz), 6.87 (1H, s), 6.97  
(1H, s), 7.14 (2H, d, J=8.9Hz), 7.24 (1H, s), 7.44 (1H,  
d, J=7.9Hz), 7.5-7.8 (2H, m), 7.89 (2H, d, J=8.9Hz),  
7.9-8.0 (6H, m), 8.12 (1H, d, J=7.7Hz), 8.60 (1H, d,  
J=7.2Hz), 8.72 (1H, s), 8.85 (1H, s)

20 MASS (m/z) : 1278 (M-Na<sup>+</sup>)Example 20

NMR (DMSO-d<sub>6</sub>, δ) : 0.91 (3H, t, J=7.3Hz), 0.96 (3H, d,  
J=7.1Hz), 1.09 (3H, d, J=5.8Hz), 1.3-1.6 (4H, m),  
1.6-2.6 (10H, m), 2.95 (1H, m), 3.1-3.5 (2H, m),  
25 3.6-4.6 (16H, m), 4.7-5.4 (8H, m), 6.71 (1H, d,  
J=8.1Hz), 6.78 (1H, d, J=8.1Hz), 6.87 (1H, s), 6.97  
(1H, s), 7.14 (2H, d, J=8.9Hz), 7.24 (1H, s), 7.44 (1H,  
d, J=7.9Hz), 7.5-7.8 (2H, m), 7.89 (2H, d, J=8.9Hz),  
7.9-8.0 (6H, m), 8.12 (1H, d, J=7.7Hz), 8.60 (1H, d,  
30 J=7.2Hz), 8.72 (1H, s), 8.85 (1H, s)

MASS (m/z) : 1338 (M+Na<sup>+</sup>)

The following compounds [Examples 21 to 29] were obtained  
according to similar manner to that of Example 1.

Example 2135 IR (KBr) : 3353, 1666.2, 1631.5, 1510, 1236 cm<sup>-1</sup>

397

NMR (DMSO-d<sub>6</sub>, δ) : 0.86 (3H, t, J=6.8Hz), 0.95 (3H, d, J=6.7Hz), 1.09 (3H, d, J=5.8Hz), 1.2-1.5 (10H, m), 1.55-2.6 (9H, m), 2.95 (1H, m), 3.0-3.5 (10H, m), 3.6-4.5 (15H, m), 4.6-5.4 (10H, m), 6.6-7.1 (10H, m), 7.27 (1H, s), 7.35-7.5 (2H, m), 7.65 (1H, br s), 7.78 (2H, d, J=8.8Hz), 8.03 (1H, d, J=8.7Hz), 8.30 (1H, d, J=8.7Hz), 8.83 (1H, s)

MASS (m/z) : 1357 (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>83</sub>N<sub>10</sub>O<sub>21</sub>SNa·5H<sub>2</sub>O :

C 50.55, H 6.58, N 9.83

Found : C 50.56, H 6.59, N 9.76

#### Example 22

IR (KBr) : 3350, 1658.5, 1633, 1278 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.86 (3H, t, J=6.7Hz), 0.96 (3H, d, J=6.7Hz), 1.11 (3H, d, J=5.7Hz), 1.2-1.4 (8H, m), 1.45-2.45 (9H, m), 2.62 (2H, t, J=7.4Hz), 2.98 (1H, m), 3.2 (1H, m), 3.25-3.5 (1H, m), 3.6-5.4 (23H, m), 6.73 (1H, d, J=8.2Hz), 6.83 (1H, dd, J=1.5 and 8.2Hz), 6.88 (1H, s), 7.05 (1H, d, J=1.5Hz), 7.31 (2H, d, J=8.2Hz), 7.1-7.5 (4H, m), 7.64 (2H, d, J=8.2Hz), 7.74 (2H, d, J=8.4Hz), 7.6-7.8 (1H, m), 7.95 (2H, d, J=8.4Hz), 8.0-8.2 (1H, m), 8.61 (1H, d, J=6.7Hz), 8.84 (1H, s)

MASS (m/z) : 1243 (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>55</sub>H<sub>73</sub>N<sub>8</sub>NaO<sub>20</sub>S·6H<sub>2</sub>O :

C 49.69, H 6.44, N 8.43

Found : C 49.99, H 6.53, N 8.40

#### Example 23

IR (Nujol) : 1668.1, 1629.6, 1540.8, 1515.8 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.87 (3H, t, J=6.7Hz), 0.95 (3H, d, J=6.7Hz), 1.07 (3H, d, J=5.9Hz), 1.25-1.48 (4H, m), 1.49-2.05 (5H, m), 2.05-2.70 (8H, m), 2.70-3.05 (3H, m), 3.08-3.45 (2H, m), 3.55-3.86 (2H, m), 3.88-4.50 (11H, m), 4.65-5.36 (10H, m), 6.67-6.90 (3H, m), 7.04 (1H, d, J=1.0Hz), 7.10-7.80 (12H, m), 8.00 (1H, d,

398

 $J=8.4\text{Hz}$ ), 8.13 (1H, d,  $J=7.7\text{Hz}$ ), 8.84 (1H, s)MASS (m/z) : 1227.5 (M+Na)<sup>+</sup>Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{73}\text{N}_8\text{NaO}_{20}\text{S}\cdot 5\text{H}_2\text{O}$  :

C 50.38, H 6.38, N 8.54

5

Found : C 50.07, H 6.60, N 8.58

Example 24IR (KBr) : 3350, 2929, 1664, 1635, 1515, 1440, 1278,  
1245, 1085, 1047  $\text{cm}^{-1}$ 

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, m), 0.96 (3H, d,  $J=7.7\text{Hz}$ ),  
1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.30 (6H, m), 1.5-2.4 (9H, m),  
2.6-2.8 (2H, t,  $J=7.2\text{Hz}$ ), 2.9-3.1 (1H, m), 3.1-3.3 (1H,  
m), 3.4-3.6 (1H, m), 3.7-4.6 (14H, m), 4.6-5.3 (9H,  
m), 6.7-7.0 (3H, m), 7.04 (1H, s), 7.21 (1H, s), 7.30  
15 (2H, d,  $J=8.2\text{Hz}$ ), 7.4-7.5 (1H, m), 7.6-7.8 (5H, m),  
7.95 (2H, d,  $J=8.4\text{Hz}$ ), 8.10 (1H, d,  $J=8.4\text{Hz}$ ), 8.60 (1H,  
d,  $J=8.4\text{Hz}$ ), 8.84 (1H, s)

MASS (m/z) : 1230 (M+Na)<sup>+</sup>Elemental Analysis Calcd. for  $\text{C}_{54}\text{H}_{71}\text{N}_8\text{NaO}_{20}\text{S}\cdot 4.5\text{H}_2\text{O}$  :

C 50.34, H 6.26, N 8.70

20

Found : C 50.43, H 6.19, N 8.59

Example 25IR (KBr) : 3350, 1666.2, 1631.5, 1510.0, 1236.1  $\text{cm}^{-1}$ 

25 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t,  $J=6.6\text{Hz}$ ), 0.95 (3H, d,  
 $J=6.7\text{Hz}$ ), 1.08 (3H, d,  $J=5.7\text{Hz}$ ), 1.2-1.5 (6H, m),  
1.6-2.1 (5H, m), 2.1-2.5 (4H, m), 2.8-3.0 (1H, m),  
3.1-3.3 (5H, m), 3.3-3.4 (4H, m), 3.6-5.4 (23H, m),  
6.73 (1H, d,  $J=8.1\text{Hz}$ ), 6.8-6.9 (4H, m), 6.94 (2H, d,  
 $J=9.3\text{Hz}$ ), 7.01 (2H, d,  $J=8.7\text{Hz}$ ), 7.04 (1H, s), 7.2-7.5  
(3H, m), 7.6-7.7 (1H, m), 7.78 (2H, d,  $J=8.7\text{Hz}$ ), 8.05  
30 (1H, d,  $J=8\text{Hz}$ ), 8.30 (1H, d,  $J=6.7\text{Hz}$ ), 8.85 (1H, s)

MASS (m/z) : 1329 (M+Na)<sup>+</sup>Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{79}\text{N}_{10}\text{O}_{21}\text{SNa}\cdot 6\text{H}_2\text{O}$  :

C 49.22, H 6.48, N 9.90

Found : C 49.46, H 6.44, N 9.96

35 Example 26

399

IR (KBr) : 3347.8, 1670.1, 1652.7, 1635.3  $\text{cm}^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85 (3H, t,  $J=6.6\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.12 (3H, d,  $J=5.9\text{Hz}$ ), 1.18-1.40 (8H, m), 1.50-2.10 (5H, m), 2.10-2.60 (4H, m), 2.76 (2H, t,  $J=7.6\text{Hz}$ ), 2.85-3.50 (3H, m), 3.60-4.60 (14H, m), 4.60-5.33 (9H, m), 6.67-7.00 (3H, m), 7.05 (1H, d,  $J=0.4\text{Hz}$ ), 7.20-7.50 (4H, m), 7.60-7.80 (2H, m), 7.85-8.00 (3H, m), 8.10 (1H, d,  $J=8.5\text{Hz}$ ), 8.45 (1H, s), 8.68 (1H, d,  $J=8.4\text{Hz}$ ), 8.48 (1H, s)

10 MASS (m/z) : 1217.4 (M+Na-1)

Elemental Analysis Calcd. for  $\text{C}_{53}\text{H}_{71}\text{N}_8\text{O}_{21}\text{SNa}\cdot 4\text{H}_2\text{O}$  :

C 49.61, H 6.20, N 8.73

Found : C 49.62, H 6.38, N 8.68

Example 2715 IR (KBr) : 3361.3, 1668.1, 1635.3  $\text{cm}^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.8\text{Hz}$ ), 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.10 (3H, d,  $J=5.9\text{Hz}$ ), 1.20-1.48 (6H, m), 1.55-2.13 (5H, m), 2.13-2.60 (4H, m), 2.76 (2H, t,  $J=7.6\text{Hz}$ ), 2.89-3.08 (1H, m), 3.10-3.50 (3H, m), 3.60-3.85 (2H, m), 3.85-4.65 (12H, m), 4.65-5.50 (8H, m), 6.62-7.05 (3H, m), 7.06 (1H, d,  $J=0.4\text{Hz}$ ), 7.15-7.55 (4H, m), 7.55-7.80 (2H, m), 7.80-8.03 (3H, m), 8.03-8.20 (1H, m), 8.45 (1H, s), 8.60-9.05 (2H, m)

20 MASS (m/z) : 1203.4 (M+Na-1)

25 Elemental Analysis Calcd. for  $\text{C}_{52}\text{H}_{69}\text{N}_8\text{NaO}_{20}\text{S}\cdot 6\text{H}_2\text{O}$  :

C 48.44, H 6.33, N 8.69

Found : C 48.55, H 6.39, N 8.70

Example 28

30 IR (KBr) : 3359.4, 1664.3, 1631.5, 1510.0, 1230.4,  
1045.2  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.5\text{Hz}$ ), 1.08 (3H, d,  $J=5.6\text{Hz}$ ), 1.2-1.6 (10H, m), 1.6-2.1 (5H, m), 2.1-2.5 (4H, m), 2.95 (1H, m), 3.0-3.2 (5H, m), 3.20 (3H, s), 3.29 (3H, t,  $J=6.4\text{Hz}$ ), 3.2-3.5 (5H, m), 3.6-4.5 (16H, m), 4.6-5.4 (9H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.8-7.1

400

(10H, m), 7.2-7.5 (2H, m), 7.70 (1H, br s), 7.78 (2H, d, J=8.6Hz), 8.10 (1H, br s), 8.32 (1H, d, J=7.2Hz), 8.90 (1H, br s)

MASS (m/z) : 1387 (M+Na)<sup>+</sup>5 Elemental Analysis Calcd. for C<sub>61</sub>H<sub>84</sub>N<sub>10</sub>O<sub>22</sub>SNa·8H<sub>2</sub>O :

C 48.53, H 6.74, N 9.28

Found : C 48.38, H 7.18, N 9.18

Example 29

IR (KBr) : 3355.5, 1666.2, 1631.5, 1608.3, 1236.1,

10 1045.2 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.93 (3H, d, J=6.6Hz), 1.07 (3H, d, J=5.7Hz), 1.2-1.6 (8H, m), 1.6-2.1 (5H, m), 2.1-2.6 (4H, m), 2.96 (1H, m), 3.1-3.3 (5H, m), 3.19 (3H, s), 3.28 (3H, t, J=6.5Hz), 3.3-3.5 (5H, m), 3.7-4.5 (16H, m), 4.65-5.3 (9H, m), 6.71 (1H, d, J=8.1Hz), 6.8-7.1 (9H, m), 7.26 (1H, s), 7.3-7.5 (2H, m), 7.66 (1H, br s), 7.76 (2H, d, J=8.6Hz), 8.07 (1H, d, J=7.7Hz), 8.31 (1H, d, J=6.8Hz), 8.83 (1H, s)

MASS (m/z) : 1373 (M+Na)<sup>+</sup>

20 The following compounds [Examples 30 to 54] were obtained in a manner similar to that of Example 8.

Example 30IR (KBr) : 3369, 2935, 1664, 1631, 1444, 1257, 1047 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 0.89 (3H, d, J=6.9Hz), 0.95 (3H, d, J=6.8Hz), 1.11 (3H, d, J=5.8Hz), 1.2-1.5 (6H, m), 1.6-2.4 (9H, m), 2.9-3.4 (2H, m), 3.6-4.5 (16H, m), 4.7-5.4 (9H, m), 6.73 (1H, d, J=8.2Hz), 6.8-7.0 (2H, m), 7.0-7.2 (4H, m), 7.3-7.7 (3H, m), 7.97 (2H, d, J=8.7Hz), 8.1-8.3 (5H, m), 8.81 (1H, d, J=7.0Hz), 8.85 (1H, s)

MASS (m/z) : 1329.8 (M+Na)<sup>+</sup>Elemental Analysis Calcd. for C<sub>56</sub>H<sub>71</sub>N<sub>10</sub>O<sub>21</sub>S<sub>2</sub>Na :

C 46.93, H 5.98, N 9.77

Found : C 46.72, H 6.11, N 9.72

35 Example 31



401

IR (KBr) : 3353, 2935, 2873, 1658, 1635, 1440, 1257,  
1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.9\text{Hz}$ ), 0.96 (3H, d,  
 $J=6.8\text{Hz}$ ), 1.12 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.5 (6H, m),  
1.6-2.4 (9H, m), 2.9-3.2 (2H, m), 3.3-3.4 (1H, m),  
3.8-4.6 (16H, m), 4.6-5.4 (9H, m), 6.7-7.0 (3H, m),  
7.0-7.2 (4H, m), 7.3-7.7 (3H, m), 7.9-8.3 (7H, m),  
8.7-8.9 (2H, m)

MASS (m/z) : 1313.0 (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{71}\text{N}_{10}\text{O}_{22}\text{S}$  :

C 48.07, H 5.98, N 10.01

Found : C 48.23, H 6.17, N 10.00

### Example 32

IR (KBr) : 3350, 2927, 1668, 1627, 1288, 1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 0.95 (3H, d,  
 $J=6.8\text{Hz}$ ), 1.13 (3H, d,  $J=6.7\text{Hz}$ ), 1.2-1.5 (10H, m),  
1.6-2.4 (8H, m), 2.9-3.2 (2H, m), 3.4-4.6 (16H, m),  
4.6-5.3 (9H, m), 6.5-7.5 (8H, m), 7.6-8.2 (4H, m), 8.31  
(1H, s), 8.43 (1H, dd,  $J=8.7$  and  $2.5\text{Hz}$ ), 8.6-8.8 (1H,  
d,  $J=6.3\text{Hz}$ ), 8.85 (1H, s), 8.99 (1H, d,  $J=2.5\text{Hz}$ )

MASS (m/z) : 1315.3 (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{73}\text{N}_{10}\text{O}_{22}\text{NaS}\cdot 7\text{H}_2\text{O}$  :

C 47.39, H 6.18, N 9.87

Found : C 47.11, H 6.29, N 9.72

### Example 33

IR (KBr) : 3350, 2925, 1670, 1625, 1259, 1047  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.7-1.0 (6H, m), 1.1-1.2 (3H, d,  
 $J=5.7\text{Hz}$ ), 1.2-2.5 (15H, m), 3.0-3.3 (2H, m), 3.4-3.6  
(1H, m), 3.6-3.8 (2H, m), 3.9-4.6 (16H, m), 4.7-5.4  
(9H, m), 6.6-7.3 (6H, m), 7.3-8.0 (5H, m), 8.0-8.3 (5H,  
m), 8.6-9.0 (2H, m)

MASS (m/z) : 1286.8 (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{70}\text{N}_9\text{O}_{22}\text{NaS}\cdot 5.5\text{H}_2\text{O}$  :

C 48.46, H 5.99, N 9.25

Found : C 48.47, H 6.01, N 9.26

Example 34MASS (m/z) : 1387 (M+Na)<sup>+</sup>Example 35IR (KBr) : 3363, 1662.3, 1631.5, 1240 cm<sup>-1</sup>

5 NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.8Hz), 0.8-1.5 (15H, m), 1.5-2.6 (16H, m), 2.8-3.5 (11H, m), 3.6-4.6 (14H, m), 4.6-5.3 (9H, m), 6.73 (1H, d, J=8.2Hz), 6.83 (1H, d, J=8.2Hz), 6.84 (1H, s), 7.00 (2H, d, J=8.8Hz), 7.04 (1H, s), 7.13 (1H, s), 7.3-7.5 (2H, m), 7.63 (1H, br s), 7.79 (2H, d, J=8.8Hz), 8.05 (1H, d, J=7.7Hz), 8.29 (1H, d, J=6.8Hz), 8.83 (1H, s)

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MASS (m/z) : 1215 (M-SO<sub>3</sub>+Na)Elemental Analysis Calcd. for C<sub>58</sub>H<sub>84</sub>N<sub>10</sub>O<sub>20</sub>S·7H<sub>2</sub>O :

C 49.78, H 7.06, N 10.01

15 Found : C 49.93, H 6.92, N 9.98

Example 36IR (KBr) : 1648, 1631 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.8Hz), 1.12 (3H, d, J=5.7Hz), 1.65-2.50 (7H, m), 2.84-3.13 (3H, m), 3.74-5.41 (23H, m), 3.83 (3H, s), 6.74 (1H, d, J=8.2Hz), 6.77 (1H, d, J=10.6Hz), 6.83 (1H, m), 7.08 (3H, m), 7.17 (1H, m), 7.43 (2H, m), 7.65 (1H, m), 7.77 (2H, d, J=8.7Hz), 7.92 (2H, d, J=8.5Hz), 8.08 (1H, m), 8.11 (2H, d, J=8.4Hz), 8.22 (2H, d, J=7.6Hz), 8.25 (2H, d, J=7.6Hz), 8.85 (2H, m)

20

25

MASS (m/z) : 1273

Elemental Analysis Calcd. for C<sub>57</sub>H<sub>65</sub>N<sub>10</sub>O<sub>22</sub>SNa·11H<sub>2</sub>O :

C 45.78, H 5.86, N 9.37

Found : C 45.75, H 5.95, N 9.27

30 Example 37

IR (KBr) : 2968, 2937, 2879, 1651, 1632 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=5.5Hz), 1.01 (3H, t, J=7.1Hz), 1.12 (3H, t, J=5.8Hz), 1.75 (2H, q, J=7.1Hz), 1.60-2.48 (7H, m), 2.75-3.10 (3H, m), 3.60-5.35 (23H, m), 4.01 (2H, t, J=7.1Hz), 6.73 (1H, d, J=8.2Hz), 6.78

35

403

(1H, d, J=9.7Hz), 6.87 (1H, m), 7.07 (3H, m), 7.16 (1H, m), 7.43 (2H, m), 7.64 (1H, m), 7.74 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.5Hz), 8.00 (1H, m), 8.10 (2H, d, J=8.5Hz), 8.21 (2H, d, J=7.4Hz), 8.25 (2H, d, J=8.3Hz), 8.83 (2H, m)

MASS (m/z) : 1301

Elemental Analysis Calcd. for  $C_{59}H_{69}N_{10}O_{22}SNa \cdot 10H_2O$  :

C 47.07, H 5.96, N 9.30

Found : C 46.88, H 5.70, N 9.14

10 Example 38IR (KBr) : 2935, 2873, 1668, 1651, 1632  $cm^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.92-0.99 (6H, m), 1.12 (3H, d,

J=6.1Hz), 1.48 (2H, qt, J=5.5 and 5.5Hz), 1.74 (2H, tt, J=5.5 and 5.5Hz), 1.60-2.40 (7H, m), 2.80-3.20 (3H, m), 4.05 (2H, t, J=5.5Hz), 3.74-5.25 (23H, m), 6.74 (1H, d, J=8.2Hz), 6.78 (1H, d, J=9.5Hz), 6.87 (1H, m), 7.07 (3H, m), 7.17 (1H, m), 7.43 (2H, m), 7.65 (1H, m), 7.70 (1H, m), 7.74 (2H, d, J=8.7Hz), 7.91 (2H, d, J=8.5Hz), 8.00 (1H, m), 8.10 (2H, d, J=8.6Hz), 8.21 (2H, d, J=7.6Hz), 8.25 (2H, d, J=8.1Hz), 8.88 (2H, m)

MASS (m/z) : 1315

Elemental Analysis Calcd. for  $C_{60}H_{71}N_{10}O_{22}SNa \cdot 9H_2O$  :

C 48.00, H 5.97, N 9.33

Found : C 48.05, H 5.95, N 9.34

25 Example 39IR (KBr) : 2943, 2870, 1668, 1651, 1632  $cm^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (6H, m), 1.13 (3H, d, J=5.7Hz), 1.39 (4H, m), 1.60-2.50 (9H, m), 2.80-3.20 (3H, m), 3.74-5.25 (23H, m), 4.04 (2H, t, J=6.3Hz), 6.74 (1H, d, J=8.2Hz), 6.78 (1H, d, J=11.2Hz), 6.88 (1H, m), 7.07 (3H, m), 7.17 (1H, m), 7.45 (2H, m), 7.67 (1H, m), 7.74 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.3Hz), 8.00 (1H, m), 8.10 (2H, d, J=8.4Hz), 8.21 (2H, d, J=7.9Hz), 8.25 (2H, d, J=7.9Hz), 8.25 (2H, d, J=7.9Hz), 8.80 (1H, m), 8.85 (1H, s)

404

MASS (m/z) : 1330, 1329

Elemental Analysis Calcd. for  $C_{61}H_{73}N_{10}O_{22}SNa \cdot 10H_2O$  :

C 47.78, H 6.11, N 9.18

Found : C 47.90, H 6.05, N 9.18

5 Example 40IR (KBr) : 2933, 2871, 1666, 1650, 1632  $cm^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t, J=6.9Hz), 0.96 (3H, d, J=6.8Hz), 1.12 (3H, d, J=5.7Hz), 1.32-1.43 (6H, m), 1.60-2.50 (9H, m), 3.02 (3H, m), 4.04 (2H, t, J=6.4Hz), 3.74-5.25 (23H, m), 6.74 (1H, d, J=8.2Hz), 6.78 (1H, d, J=11.1Hz), 6.88 (1H, m), 7.07 (3H, m), 7.17 (1H, m), 7.43 (2H, m), 7.67 (1H, m), 7.75 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.5Hz), 8.00 (1H, m), 8.11 (2H, d, J=8.5Hz), 8.20 (2H, d, J=7.9Hz), 8.25 (2H, d, J=8.1Hz), 8.84 (2H, m)

MASS (m/z) : 1343, 1327

Elemental Analysis Calcd. for  $C_{62}H_{75}N_{10}O_{22}SNa \cdot 7H_2O$  :

C 49.86, H 6.01, N 9.38

Found : C 49.87, H 6.01, N 9.30

20 Example 41IR (KBr) : 2931, 2858, 1651, 1632  $cm^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88 (3H, t, J=6.6Hz), 0.96 (3H, d, J=6.7Hz), 1.12 (3H, d, J=5.2Hz), 1.30 (8H, m), 1.60-2.40 (9H, m), 2.80-3.20 (3H, m), 4.03 (2H, t, J=6.3Hz), 3.74-5.25 (23H, m), 6.72 (1H, d, J=8.2Hz), 6.78 (1H, d, J=9.7Hz), 6.87 (1H, m), 7.06 (3H, m), 7.16 (1H, m), 7.44 (2H, m), 7.70 (1H, m), 7.74 (2H, d, J=8.8Hz), 7.90 (2H, d, J=8.5Hz), 8.00 (1H, m), 8.10 (2H, d, J=8.6Hz), 8.20 (2H, d, J=7.8Hz), 8.25 (2H, d, J=8.2Hz), 8.84 (2H, m)

MASS (m/z) : 1361, 1357, 1341

Elemental Analysis Calcd. for  $C_{63}H_{77}N_{10}O_{22}SNa \cdot 6H_2O$  :

C 50.80, H 6.02, N 9.40

Found : C 50.79, H 6.28, N 9.48

35 Example 42

405

IR (KBr) : 2939, 1668, 1651, 1632  $\text{cm}^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=5.3\text{Hz}$ ), 1.13 (3H, d,  $J=6.0\text{Hz}$ ), 1.35-2.50 (15H, m), 2.60-3.20 (9H, m), 3.65-5.40 (25H, m), 6.73 (1H, d,  $J=8.5\text{Hz}$ ), 6.78 (1H, d,  $J=11.2\text{Hz}$ ), 6.88 (1H, m), 7.09 (3H, m), 7.17 (1H, m), 7.44 (2H, m), 7.70 (1H, m), 7.76 (2H, d,  $J=7.1\text{Hz}$ ), 7.91 (2H, d,  $J=6.6\text{Hz}$ ), 8.08 (1H, m), 8.11 (2H, d,  $J=7.4\text{Hz}$ ), 8.22 (2H, d,  $J=6.1\text{Hz}$ ), 8.25 (2H, d,  $J=6.3\text{Hz}$ ), 8.84 (2H, m)

10 MASS (m/z) : 1388, 1384, 1368

Elemental Analysis Calcd. for  $\text{C}_{64}\text{H}_{78}\text{N}_{11}\text{O}_{22}\text{SNa}\cdot 7\text{H}_2\text{O}$  :

C 50.09, H 6.04, N 10.04

Found : C 50.18, H 6.03, N 9.65

Example 4315 IR (KBr) : 1650.8, 1629.6  $\text{cm}^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.80-0.86 (3H, m), 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.12 (3H, d,  $J=5.6\text{Hz}$ ), 1.23 (14H, br s), 1.74-2.50 (9H, m), 2.98 (1H, d,  $J=13.4\text{Hz}$ ), 3.10-3.46 (2H, m), 3.70-4.60 (16H, m), 4.64-5.32 (9H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.4\text{Hz}$ ), 6.89 (1H, br s), 7.05 (1H, d,  $J=1.7\text{Hz}$ ), 7.16 (1H, br s), 7.42-7.47 (2H, m), 7.66 (1H, br s), 8.06-8.17 (6H, m), 8.65 (1H, s), 8.80 (1H, d,  $J=7.5\text{Hz}$ ), 8.84 (1H, s)

25 MASS (m/z) : 1297.03 (M-Na) $^{+}$ Elemental Analysis Calcd. for  $\text{C}_{57}\text{H}_{77}\text{N}_{12}\text{O}_{21}\text{SNa}\cdot 7\text{H}_2\text{O}$  :

C 47.30, H 6.34, N 11.61

Found : C 47.33, H 6.16, N 11.54

Example 4430 IR (KBr) : 3361.3, 1650.8, 1631.5  $\text{cm}^{-1}$ 

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.80-0.90 (3H, m), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.15 (3H, d,  $J=6\text{Hz}$ ), 1.23 (14H, br s), 1.70-2.65 (9H, m), 2.90-3.10 (1H, m), 3.20-3.42 (2H, m), 3.65-4.60 (16H, m), 4.66-5.40 (9H, m), 6.73 (1H, d,  $J=8.3\text{Hz}$ ), 6.83 (1H, d,  $J=8.8\text{Hz}$ ), 6.89 (1H, s), 7.05 (1H, s), 7.18 (1H, s), 7.42-7.46 (2H, m), 7.66 (1H,

406

br s), 8.05 (4H, s), 8.08 (1H, s), 8.57 (1H, s),  
8.57-8.84 (3H, m)

MASS (m/z) : 1313.01 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>57</sub>H<sub>77</sub>N<sub>12</sub>O<sub>20</sub>S<sub>2</sub>Na·7H<sub>2</sub>O :

5 C 46.78, H 6.27, N 11.48

Found : C 46.89, H 6.34, N 11.41

Example 45

IR (KBr) : 1650.8, 1631.5 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d,  
J=6Hz), 1.70-2.60 (9H, m), 2.80-3.60 (3H, m),  
3.60-4.60 (19H, m), 4.65-5.40 (8H, m), 6.73 (1H, d,  
J=8.2Hz), 6.81-6.99 (6H, m), 7.05 (1H, s), 7.11 (2H,  
d, J=8.8Hz), 7.34-7.26 (2H, m), 7.34-7.73 (3H, m), 7.76  
15 (2H, d, J=8.8Hz), 7.91 (2H, d, J=8.4Hz), 8.11 (2H, d,  
J=8.4Hz), 8.19-8.30 (4H, m), 8.70-9.00 (3H, m)

MASS (m/z) : 1393.13 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>65</sub>H<sub>73</sub>N<sub>10</sub>O<sub>23</sub>SNa·9H<sub>2</sub>O :

C 49.43, H 5.81, N 8.87

Found : C 49.24, H 5.61, N 8.77

20 Example 46

IR (KBr) : 3361.3, 1668.1, 1650.8, 1631.5 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.6Hz), 1.12 (3H, d,  
J=5.6Hz), 1.70-2.60 (7H, m), 2.80-5.27 (26H, m), 4.65  
(2H, d, J=5.2Hz), 5.27-5.48 (2H, m), 5.99-6.18 (1H,  
m), 6.72 (1H, d, J=8.1Hz), 6.82 (1H, d, J=8.1Hz), 6.89  
(1H, s), 7.07 (1H, s), 7.10 (2H, d, J=8.8Hz), 7.12 (1H,  
s), 7.46 (2H, br s), 7.68 (1H, br s), 7.75 (2H, d,  
J=8.7Hz), 7.91 (2H, d, J=8.4Hz), 8.11 (2H, d, J=8.5Hz),  
8.19-8.31 (4H, m), 8.80-8.83 (2H, m)

30 MASS (m/z) : 1298.97 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>59</sub>H<sub>67</sub>N<sub>10</sub>O<sub>2</sub>SNa·9H<sub>2</sub>O :

C 47.71, H 5.77, N 9.43

Found : C 47.90, H 5.61, N 9.41

Example 47

35 IR (KBr) : 1650.8, 1631.5, 1540.8, 1513.8 cm<sup>-1</sup>

407

5 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.12 (3H, d, J=5.7Hz), 1.70-2.60 (11H, m), 2.80-3.60 (3H, m), 3.60-4.60 (18H, m), 4.65-5.40 (9H, m), 6.73 (1H, d, J=8.1Hz), 6.82 (1H, d, J=9.5Hz), 6.87-6.97 (5H, m), 7.06 (1H, s), 7.09 (2H, d, J=8.8Hz), 7.25-7.33 (2H, m), 7.33-7.73 (3H, m), 7.75 (2H, d, J=8.6Hz), 7.91 (2H, d, J=8.5Hz), 8.11 (2H, d, J=8.5Hz), 8.19-8.27 (4H, m), 8.70-8.90 (3H, m)

MASS (m/z) : 1407.15 (M-Na)<sup>+</sup>  
Elemental Analysis Calcd. for C<sub>66</sub>H<sub>75</sub>N<sub>10</sub>O<sub>23</sub>SNa·7H<sub>2</sub>O :  
C 50.90, H 5.76, N 8.99  
Found : C 50.80, H 5.90, N 8.90

### Example 48

IR (KBr) : 1675.8, 1650.8, 1540.8, 1513.8  $\text{cm}^{-1}$   
15 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.9\text{Hz}$ ), 1.13 (3H, d,  $J=5.9\text{Hz}$ ), 1.20-1.60 (12H, m), 1.64-2.68 (7H, m), 2.80-3.60 (3H, m), 3.21 (3H, s), 3.60-5.40 (27H, m), 6.73 (1H, d,  $J=8.4\text{Hz}$ ), 6.83 (1H, d,  $J=9.3\text{Hz}$ ), 6.89 (1H, s), 7.05 (1H, s), 7.07 (2H, d,  $J=8.7\text{Hz}$ ), 7.17 (1H, s),  
20 7.30-7.70 (3H, m), 7.74 (2H, d,  $J=8.7\text{Hz}$ ), 7.91 (2H, d,  $J=8.4\text{Hz}$ ), 8.11 (2H, d,  $J=8.5\text{Hz}$ ), 8.19-8.27 (4H, m), 8.74-8.90 (3H, m)

MASS (m/z) : 1401.12 (M-Na)<sup>+</sup>

### Example 49

25 IR (KBr) : 1675.8, 1650.8, 1540.8  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.4\text{Hz}$ ), 1.03-1.10  
(9H, m), 1.50-2.50 (11H, m), 2.70-5.50 (34H, m), 6.71  
(1H, d,  $J=7.3\text{Hz}$ ), 6.79-6.90 (2H, m), 7.00-7.10 (4H,  
m), 7.30-7.80 (3H, m), 7.75 (2H, d,  $J=8.6\text{Hz}$ ), 7.91 (2H,  
30 d,  $J=8.4\text{Hz}$ ), 8.11 (2H, d,  $J=7.4\text{Hz}$ ), 8.19-8.27 (4H, m),  
8.60-8.90 (3H, m)

MASS (m/z) : 1414.08 (M-Na)<sup>+</sup>  
Elemental Analysis Calcd. for C<sub>65</sub>H<sub>80</sub>N<sub>11</sub>O<sub>23</sub>SNa·11.6H<sub>2</sub>O :  
C 47.39, H 6.31, N 9.35  
Found : C 47.40, H 6.07, N 9.22

Example 50

IR (KBr) : 3353.6, 1650.8, 1631.5, 1538.9, 1515.8,  
1442.5, 1114.7  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.12 (3H, d,  
 $J=5.7\text{Hz}$ ), 1.7-2.6 (11H, m), 2.9-3.1 (1H, m), 3.1-3.5  
(2H, m), 3.7-4.6 (18H, m), 4.7-5.3 (9H, m), 6.74 (1H,  
d,  $J=8.0\text{Hz}$ ), 6.83 (1H, d,  $J=8.0\text{Hz}$ ), 6.87-7.02 (4H, m),  
7.05 (1H, s), 7.15 (2H, d,  $J=8.7\text{Hz}$ ), 7.17 (1H, m),  
10 7.2-7.4 (2H, m), 7.4-7.6 (2H, m), 7.67 (1H, br), 7.98  
(2H, d,  $J=8.7\text{Hz}$ ), 7.9-8.2 (5H, m), 8.77 (1H, d,  
 $J=8.5\text{Hz}$ ), 8.84 (1H, s)

MASS (m/z) : 1346.72 (M-Na) $^{+}$

Elemental Analysis Calcd. for  $\text{C}_{60}\text{H}_{71}\text{N}_{10}\text{NaO}_{22}\text{S}\cdot 11\text{H}_2\text{O}$  :

C 45.92, H 5.97, N 8.92

15 Found : C 46.13, H 5.75, N 8.92

Example 51

IR (KBr) : 3363.2, 1650.8, 1538.9, 1515.8, 1442.5,  
1247.7  $\text{cm}^{-1}$

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.12 (3H, d,  
 $J=5.9\text{Hz}$ ), 1.5-2.5 (13H, m), 2.9-3.1 (1H, m), 3.1-3.5  
(2H, m), 3.6-5.4 (27H, m), 6.73 (1H, d,  $J=8.2\text{Hz}$ ), 6.82  
(1H, d,  $J=8.2\text{Hz}$ ), 6.87-7.00 (4H, m), 7.05 (1H, s), 7.14  
(2H, d,  $J=8.7\text{Hz}$ ), 7.16 (1H, s), 7.27 (2H, m), 7.42 (2H,  
m), 7.66 (1H, br), 7.97 (2H, d,  $J=8.7\text{Hz}$ ), 7.9-8.2 (5H,  
25 m), 8.7-8.9 (2H, m)

MASS (m/z) : 1360.75 (M-Na) $^{+}$

Elemental Analysis Calcd. for  $\text{C}_{61}\text{H}_{73}\text{N}_{10}\text{NaO}_{22}\text{S}_2\cdot 9\text{H}_2\text{O}$  :

C 47.34, H 5.93, N 9.05

Found : C 47.27, H 5.76, N 8.94

30 Example 52

IR (KBr) : 3365.2, 1650.8, 1631.5, 1538.9, 1515.8,  
1442.5, 1245.8  $\text{cm}^{-1}$

35 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.12 (3H, d,  
 $J=5.6\text{Hz}$ ), 1.7-2.7 (9H, m), 2.9-3.1 (1H, m), 3.1-3.5  
(2H, m), 3.6-4.6 (18H, m), 4.6-5.5 (9H, m), 6.73 (1H,



409

d,  $J=8.3\text{Hz}$ ), 6.83 (1H, d,  $J=8.3\text{Hz}$ ), 6.84-7.00 (4H, m),  
7.05 (1H, s), 7.17 (2H, d,  $J=8.7\text{Hz}$ ), 7.19 (1H, m),  
7.2-7.6 (4H, m), 7.67 (1H, br), 7.98 (2H, d,  $J=8.7\text{Hz}$ ),  
7.8-8.2 (5H, m), 8.6-9.0 (2H, m)

5      MASS (m/z) : 1332.97 (M-Na)<sup>+</sup>  
         Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{69}\text{N}_{10}\text{NaO}_{22}\text{S}\cdot 8\text{H}_2\text{O}$  :  
   C 47.20, H 5.71, N 9.33  
   Found :    C 47.10, H 5.59, N 9.24

Example 53

10      IR (KBr) : 3353.6, 1650.8, 1631.5, 1538.9, 1513.8,  
   1450.2, 1442.5, 1257.4  $\text{cm}^{-1}$   
         NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.12 (3H, d,  
    $J=5.7\text{Hz}$ ), 1.3-2.6 (13H, m), 2.9-3.1 (1H, m), 3.1-3.6  
   (7H, m), 3.6-4.6 (16H, m), 4.6-5.5 (9H, m), 6.73 (1H,  
15      d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.89 (1H, s), 7.05  
   (1H, s), 7.13 (2H, d,  $J=8.8\text{Hz}$ ), 7.15 (1H, m), 7.3-  
   7.8 (3H, m), 7.97 (2H, d,  $J=8.8\text{Hz}$ ), 7.8-8.2 (5H, m),  
   8.6-9.0 (2H, br)  
         MASS (m/z) : 1298.85 (M-Na)<sup>+</sup>  
20      Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{71}\text{N}_{10}\text{NaO}_{22}\text{S}\cdot 10\text{H}_2\text{O}$  :  
   C 44.74, H 6.10, N 9.32  
   Found :    C 44.78, H 5.96, N 9.27

Example 54

25      IR (KBr) : 3365, 1647, 1541, 1516, 1437, 1248, 1047  $\text{cm}^{-1}$   
         NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.12 (3H, d,  
    $J=5.6\text{Hz}$ ), 1.49-1.74 (6H, m), 1.74-2.55 (7H, m),  
   2.90-3.50 (3H, m), 3.60-3.85 (6H, m), 3.85-4.59 (13H,  
   m), 4.70-5.40 (8H, m), 6.74 (1H, d,  $J=8.2\text{Hz}$ ), 6.81 (1H,  
   s), 6.87 (1H, d,  $J=8.2\text{Hz}$ ), 6.99 (1H, d,  $J=9.1\text{Hz}$ ), 7.06  
30      (1H, s), 7.19 (1H, s), 7.35-7.50 (2H, m), 7.68 (1H,  
   m), 8.05 (1H, m), 8.06 (4H, s), 8.08 (1H, dd,  $J=9.1$   
   and  $2.5\text{Hz}$ ), 8.71 (1H, d,  $J=2.5\text{Hz}$ ), 8.77 (1H, d,  
    $J=7.4\text{Hz}$ ), 8.82 (1H, br s)  
         MASS (m/z) : 1266.93 (M-Na)<sup>+</sup>  
35      Elemental Analysis Calcd. for  $\text{C}_{54}\text{H}_{67}\text{N}_{12}\text{NaO}_{20}\text{S}_2\cdot 10\text{H}_2\text{O}$  :

410

C 44.08, H 5.96, N 11.42

Found : C 44.28, H 5.81, N 11.48

The following compounds [Examples 55 and 56] were obtained in a manner similar to that of Example 17.

5 Example 55IR (KBr) : 3359, 1651, 1539, 1522  $\text{cm}^{-1}$ 

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.8-1.0 (6H, m), 1.11 (3H, d,  $J=5.5\text{Hz}$ ), 1.3-1.6 (4H, m), 1.6-2.15 (5H, m), 2.2-2.5 (4H, m), 2.97 (1H, m), 3.20 (1H, m), 3.74 (2H, m), 3.8-4.6 (14H, m), 4.6-5.4 (10H, m), 6.74 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.89 (1H, s), 7.05 (1H, s), 7.22 (1H, m), 7.45 (3H, m), 7.52 (2H, d,  $J=4.9\text{Hz}$ ), 7.66 (1H, m), 7.96 (5H, m), 8.08 (1H, d,  $J=8.2\text{Hz}$ ), 8.59 (1H, d,  $J=6.4\text{Hz}$ ), 8.85 (1H, s), 8.89 (1H, s)

MASS (m/z) : 1307.69 (M-Na) $^{+}$ Elemental Analysis Calcd. for  $\text{C}_{57}\text{H}_{70}\text{N}_{11}\text{O}_{21}\text{S}_2\text{Na}\cdot 10\text{H}_2\text{O}$  :

C 45.26, H 6.00, N 10.19

Found : C 45.11, H 5.84, N 10.28

20 Example 56IR (KBr) : 3359, 1651, 1539, 1524, 1458, 1254  $\text{cm}^{-1}$ 

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.6\text{Hz}$ ), 1.12 (3H, d,  $J=5.5\text{Hz}$ ), 1.2-1.6 (6H, m), 1.6-2.1 (7H, m), 2.1-2.4 (4H, m), 2.96 (1H, m), 3.19 (1H, m), 3.42 (1H, m), 3.74 (2H, m), 3.8-4.6 (12H, m), 4.73 (1H, m), 4.8-5.0 (3H, m), 5.06 (1H, d,  $J=5.8\text{Hz}$ ), 5.1-5.3 (5H, m), 6.74 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.89 (1H, s), 7.05 (1H, s), 7.15 (2H, d,  $J=8.8\text{Hz}$ ), 7.23 (1H, s), 7.3-7.5 (2H, m), 7.66 (1H, s), 7.88 (2H, d,  $J=8.8\text{Hz}$ ), 7.95 (4H, s), 8.07 (1H, d,  $J=7.8\text{Hz}$ ), 8.58 (1H, d,  $J=7.8\text{Hz}$ ), 8.85 (2H, s)

MASS (m/z) : 1319.74 (M-Na) $^{+}$ Elemental Analysis Calcd. for  $\text{C}_{58}\text{H}_{70}\text{N}_{11}\text{O}_{21}\text{S}_2\text{Na}\cdot 10\text{H}_2\text{O}$  :

C 45.70, H 5.95, N 10.11

Found : C 45.58, H 5.80, N 10.13

The following compounds [Examples 57 to 60] were obtained in a manner similar to that of Example 18.

Example 57

IR (KBr) : 3350, 2929, 1664, 1629, 1446, 1284,  
5 1047.2  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.07 (3H, d,  $J=5.9\text{Hz}$ ), 1.2-1.5 (10H, m), 1.6-2.5 (9H, m), 2.9-3.5 (4H, m), 3.7-4.5 (16H, m), 4.7-4.8 (1H, m), 4.87 (1H, d,  $J=5.9\text{Hz}$ ), 5.0-5.4 (5H, 10 m), 6.7-6.9 (4H, m), 6.96 (1H, s), 7.17 (1H, s), 7.40 (1H, d,  $J=8.4\text{Hz}$ ), 7.5-7.8 (2H, m), 8.0-8.2 (2H, m), 8.61 (1H, d,  $J=7.7\text{Hz}$ ), 8.68 (1H, d,  $J=8.9\text{Hz}$ )  
MASS (m/z) : 1182.4 (M+Na)<sup>+</sup>  
Elemental Analysis Calcd. for  $\text{C}_{49}\text{H}_{70}\text{N}_9\text{NaO}_{20}\text{S}\cdot 4\text{H}_2\text{O}$  :  
15 C 47.76, H 6.38, N 10.23  
Found : C 47.81, H 6.73, N 10.12

Example 58

IR (KBr) : 3349, 2929, 1664, 1633, 1535, 1515, 1440,  
1272, 1045  $\text{cm}^{-1}$   
20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.86 (3H, t,  $J=6.8\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.10 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.4 (8H, m), 1.5-2.5 (10H, m), 2.58 (2H, t,  $J=7.6\text{Hz}$ ), 2.9-3.1 (1H, m), 3.2-3.6 (3H, m), 3.7-4.2 (5H, m), 4.1-4.6 (8H, m), 4.7-5.2 (7H, m), 5.3-5.4 (1H, m), 6.7-7.8 (14H, m), 25 7.95 (2H, d,  $J=8.3\text{Hz}$ ), 8.10 (1H, d,  $J=8.4\text{Hz}$ ), 8.63 (1H, d,  $J=7.7\text{Hz}$ ), 8.71 (1H, s)  
MASS (m/z) : 1227.5 (M+Na)<sup>+</sup>  
Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{73}\text{N}_8\text{NaO}_{19}\text{S}\cdot 5\text{H}_2\text{O}$  :  
C 51.00, H 6.46, N 8.65  
30 Found : C 50.90, H 6.54, N 8.81

Example 59

IR (Nujol) : 3353.0, 1668.1, 1629.6, 1540.8, 1515.8  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87 (3H, t,  $J=6.7\text{Hz}$ ), 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.06 (3H, d,  $J=6.0\text{Hz}$ ), 1.18-1.48 (4H, m), 35 1.48-2.06 (5H, m), 2.06-2.70 (8H, m), 2.70-3.08 (3H,

412

m), 3.09-3.50 (2H, m), 3.60-4.65 (14H, m), 4.65-5.50 (9H, m), 6.65-6.90 (3H, m), 6.90-7.90 (13H, m), 8.02 (1H, d, J=8.4Hz), 8.15 (1H, d, J=7.7Hz), 8.71 (1H, s)

MASS (m/z) : 1227.5 (M+Na)<sup>+</sup>

5 Elemental Analysis Calcd. for C<sub>55</sub>H<sub>73</sub>N<sub>8</sub>NaO<sub>19</sub>S·5H<sub>2</sub>O :

C 50.99, H 6.46, N 8.65

Found : C 50.84, H 6.62, N 8.81

#### Example 60

IR (KBr) : 3353.6, 1635.3, 1257.4 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 0.89 (3H, t, J=6.8Hz), 0.97 (3H, d, J=6.7Hz), 1.09 (3H, d, J=5.7Hz), 1.2-1.5 (6H, m), 1.65-2.6 (10H, m), 2.97 (1H, m), 3.1-3.5 (2H, m), 3.6-4.6 (16H, m), 4.7-5.4 (8H, m), 6.71 (1H, d, J=8.2Hz), 6.79 (1H, d, J=8.2Hz), 6.87 (1H, s), 6.97 (1H, s), 7.13 (2H, d, J=8.9Hz), 7.16 (1H, s), 7.4-7.8 (3H, m), 7.97 (2H, d, J=8.9Hz), 7.9-8.2 (5H, m), 8.72 (1H, s), 8.78 (1H, d, J=7.1Hz)

MASS (m/z) : 1267 (M-Na)<sup>+</sup>

20 The following compounds [Examples 61 to 72] were obtained in a manner similar to that of Example 13.

#### Example 61

IR (KBr) : 1650.8, 1631.5 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 0.80-0.87 (3H, s), 0.97 (3H, d, J=6.8Hz), 1.10 (3H, d, J=5.9Hz), 1.23 (14H, br s), 1.73-2.65 (10H, m), 2.92-3.50 (3H, m), 3.60-4.60 (16H, m), 4.70-5.50 (8H, m), 6.71 (1H, d, J=8.2Hz), 6.77-6.81 (1H, m), 6.86 (1H, s), 6.97 (1H, s), 7.07-7.86 (4H, m), 8.11 (1H, s), 8.06-8.17 (4H, m), 8.66 (1H, s), 8.66-8.88 (3H, m)

30 MASS (m/z) : 1326.62 (M+Na)<sup>+</sup>

Elemental Analysis Calcd. for C<sub>57</sub>H<sub>77</sub>N<sub>12</sub>O<sub>20</sub>SNa·7H<sub>2</sub>O :

C 47.83, H 6.41, N 11.74

Found : C 47.77, H 6.45, N 11.62

#### Example 62

35 IR (KBr) : 1668.1, 1650.8, 1631.5 cm<sup>-1</sup>

413

NMR (DMSO-d<sub>6</sub>, δ) : 0.81-0.90 (3H, m), 0.97 (3H, d, J=6.7Hz), 1.10 (3H, d, J=6Hz), 1.23 (14H, br s), 1.75-2.70 (10H, m), 2.95-3.02 (1H, m), 3.17-3.30 (2H, m), 3.60-4.60 (16H, m), 4.70-5.46 (8H, m), 6.71 (1H, d, J=8.2Hz), 6.79 (1H, d, J=8.5Hz), 6.87 (1H, br s), 6.98 (1H, s), 7.18 (1H, br s), 7.40-7.80 (3H, m), 8.05-8.10 (4H, m), 8.08 (1H, s), 8.57 (1H, s), 8.71-8.80 (3H, m)

MASS (m/z) : 1297.14 (M-Na)<sup>+</sup>  
Elemental Analysis Calcd. for C<sub>57</sub>H<sub>77</sub>N<sub>12</sub>O<sub>19</sub>S<sub>2</sub>Na·7H<sub>2</sub>O :  
C 47.30, H 6.34, N 11.61  
Found : C 47.07, H 6.23, N 11.42

#### Example 63

IR (KBr) : 1675.8, 1650.8 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.6Hz), 1.11 (3H, d, J=6.4Hz), 1.70-2.60 (10H, m), 2.90-3.60 (3H, m), 3.60-4.60 (18H, m), 4.68-5.60 (8H, m), 6.70 (1H, d, J=8.3Hz), 6.78 (1H, d, J=9.7Hz), 6.87 (1H, s), 6.93-6.99 (4H, m), 7.11 (2H, d, J=8.8Hz), 7.26-7.34 (2H, m), 7.09-7.78 (4H, m), 7.76 (2H, d, J=8.7Hz), 7.91 (2H, d, J=8.5Hz), 8.12 (2H, d, J=8.6Hz), 8.19-8.27 (4H, m), 8.60-9.00 (3H, m)

MASS (m/z) : 1377.26 (M-Na)<sup>+</sup>  
Elemental Analysis Calcd. for C<sub>65</sub>H<sub>73</sub>N<sub>10</sub>O<sub>22</sub>SNa·6H<sub>2</sub>O :  
C 51.72, H 5.68, N 9.28  
Found : C 51.54, H 5.73, N 9.25

#### Example 64

IR (KBr) : 1675.8, 1650.8, 1631.5 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.7Hz), 1.11 (3H, d, J=5.6Hz), 1.70-2.60 (8H, m), 2.80-3.60 (3H, m), 3.60-5.26 (22H, m), 4.65 (2H, d, J=5.2Hz), 5.26-5.48 (2H, m), 5.99-6.18 (1H, m), 6.70 (1H, d, J=8Hz), 6.78 (1H, d, J=9.9Hz), 6.87 (1H, s), 6.97 (1H, s), 7.00-7.20 (1H, m), 7.10 (2H, d, J=8.9Hz), 7.30-7.80 (3H, m), 7.75 (2H, d, J=8.9Hz), 7.92 (2H, d, J=8.5Hz), 8.12 (2H, d,

414

$J=8.6\text{Hz}$ ), 8.19-8.27 (5H, m), 8.50-9.00 (2H, m)

MASS (m/z) : 1282.84 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{67}\text{N}_{10}\text{O}_{21}\text{SNa}\cdot 7\text{H}_2\text{O}$  :

C 49.44, H 5.70, N 9.77

5 Found : C 49.33, H 5.64, N 9.74

Example 65

IR (KBr) : 1650.8, 1631.5, 1540.8, 1513.8, 1245.8  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,

10  $J=5.9\text{Hz}$ ), 1.80-2.60 (11H, m), 2.80-3.60 (3H, m),  
3.65-4.60 (19H, m), 4.63-5.50 (8H, m), 6.70 (1H, d,  
 $J=8\text{Hz}$ ), 6.77 (1H, d,  $J=7.9\text{Hz}$ ), 6.87-6.97 (5H, m),  
7.02-7.22 (1H, m), 7.09 (2H, d,  $J=8\text{Hz}$ ), 7.25-7.33 (2H,  
m), 7.40-7.80 (3H, m), 7.75 (2H, d,  $J=8.9\text{Hz}$ ), 7.91 (2H,  
d,  $J=8.5\text{Hz}$ ), 8.11 (2H, d,  $J=8.4\text{Hz}$ ), 8.23-8.27 (4H, m),  
15 8.50-9.00 (3H, m)

MASS (m/z) : 1391.07 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{66}\text{H}_{75}\text{N}_{10}\text{O}_{22}\text{SNa}\cdot 7\text{H}_2\text{O}$  :

C 51.42, H 5.82, N 9.09

Found : C 51.37, H 5.78, N 9.05

20 Example 66

IR (KBr) : 3353.6, 2939.0, 1650.8, 1631.5, 1538.9,

1513.8, 1442.5  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.10 (3H, d,

25  $J=5.7\text{Hz}$ ), 1.7-2.6 (12H, m), 2.9-3.1 (1H, m), 3.1-3.7  
(2H, m), 3.7-4.7 (18H, m), 4.7-5.5 (8H, m), 6.71 (1H,  
d,  $J=8.0\text{Hz}$ ), 6.78 (1H, d,  $J=8.0\text{Hz}$ ), 6.83-7.05 (5H, m),  
7.15 (2H, d,  $J=8.7\text{Hz}$ ), 7.17 (1H, m), 7.2-7.35 (2H, m),  
7.35-7.9 (3H, m), 7.98 (2H, d,  $J=8.7\text{Hz}$ ), 7.9-8.2 (5H,  
m), 8.75 (1H, br), 8.80 (1H, d,  $J=7.0\text{Hz}$ )

30 MASS (m/z) : 1331.28 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{60}\text{H}_{71}\text{N}_{10}\text{NaO}_{21}\text{S}_2\cdot 9\text{H}_2\text{O}$  :

C 47.49, H 5.91, N 9.23

Found : C 47.41, H 5.71, N 9.17

Example 67

35 IR (KBr) : 3353.6, 1666.2, 1650.8, 1631.5, 1538.9,

415

- 1513.8, 1442.5, 1247.7  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.10 (3H, d,  $J=5.7\text{Hz}$ ), 1.4-2.7 (14H, m), 2.9-3.1 (1H, m), 3.1-3.5 (2H, m), 3.6-4.6 (18H, m), 4.7-5.5 (8H, m), 6.71 (1H, d,  $J=8.1\text{Hz}$ ), 6.79 (1H, d,  $J=8.1\text{Hz}$ ), 6.84-7.00 (5H, m), 7.14 (2H, d,  $J=8.7\text{Hz}$ ), 7.16 (1H, m), 7.27 (2H, m), 7.44 (1H, d,  $J=8.6\text{Hz}$ ), 7.59 (1H, br), 7.71 (1H, br), 7.98 (2H, d,  $J=8.7\text{Hz}$ ), 7.9-8.2 (5H, m), 8.75 (1H, br), 8.79 (1H, d,  $J=7.2\text{Hz}$ )
- 10 MASS (m/z) : 1345.3 (M-Na) $^{+}$   
Elemental Analysis Calcd. for  $\text{C}_{61}\text{H}_{73}\text{N}_{10}\text{NaO}_{21}\text{S}_2 \cdot 8\text{H}_2\text{O}$  :  
C 48.41, H 5.93, N 9.25  
Found : C 48.30, H 5.91, N 9.17

Example 68

- 15 IR (KBr) : 3353.6, 2937.1, 1650.8, 1540.8, 1513.8,  
1452.1, 1243.9  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.7-2.7 (10H, m), 2.9-3.1 (1H, m), 3.1-3.6 (2H, m), 3.6-4.7 (18H, m), 4.7-5.5 (8H, m), 6.71 (1H, d,  $J=8.1\text{Hz}$ ), 6.79 (1H, d,  $J=8.1\text{Hz}$ ), 6.84-7.10 (5H, m), 7.17 (2H, d,  $J=8.7\text{Hz}$ ), 7.19 (1H, m), 7.2-7.4 (2H, m), 7.44 (1H, d,  $J=9.2\text{Hz}$ ), 7.5-7.9 (2H, m), 7.98 (2H, d,  $J=8.7\text{Hz}$ ), 7.9-8.2 (5H, m), 8.6-9.0 (2H, m)
- 20 MASS (m/z) : 1316.8 (M-Na) $^{+}$   
Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{69}\text{N}_{10}\text{NaO}_{21}\text{S}_2 \cdot 9\text{H}_2\text{O}$  :  
C 47.13, H 5.83, N 9.32  
Found : C 47.40, H 5.67, N 9.30

Example 69

- IR (KBr) : 3361.3, 2937.1, 1650.8, 1631.5, 1538.9,  
1513.8, 1450.2, 1440.6, 1257.4  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.99 (3H, m), 1.11 (3H, m), 1.3-2.7 (14H, m), 2.9-3.1 (1H, m), 3.1-3.6 (7H, m), 3.6-4.7 (16H, m), 4.7-5.6 (8H, m), 6.69 (1H, d,  $J=8.2\text{Hz}$ ), 6.77 (1H, d,  $J=8.2\text{Hz}$ ), 6.86 (1H, s), 6.98 (1H, s), 7.13 (2H, d,  $J=8.7\text{Hz}$ ), 7.15 (1H, m), 7.3-7.9 (3H, m), 7.97 (2H,
- 30  
35

416

d,  $J=8.7\text{Hz}$ ), 7.9-8.2 (5H, m), 8.6-8.9 (2H, m)

MASS (m/z) : 1283.2 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{71}\text{N}_{10}\text{NaO}_{21}\text{S}_2 \cdot 10\text{H}_2\text{O}$  :

C 45.22, H 6.17, N 9.42

5 Found : C 45.30, H 5.90, N 9.38

#### Example 70

IR (KBr) : 3400, 1651, 1541, 1261  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95-5.40 (58H, m), 6.67-8.77 (19H, m)

MASS (m/z) : 1325.29 (M-Na)<sup>+</sup>

10 Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{77}\text{N}_{10}\text{NaO}_{21}\text{S}_2 \cdot 37/4\text{H}_2\text{O}$  :

C 46.74, H 6.35, N 9.24

Found : C 46.74, H 6.10, N 9.15

#### Example 71

IR (KBr) : 3363, 1648, 1619, 1506, 1257  $\text{cm}^{-1}$

15 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, t,  $J=3.3\text{Hz}$ ), 1.02 (3H, d,  $J=7.3\text{Hz}$ ), 1.11 (3H, d,  $J=5.5\text{Hz}$ ), 1.68-5.40 (38H, m), 6.69-8.86 (22H, m)

MASS (m/z) : 1254 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{69}\text{N}_{10}\text{NaO}_{21}\text{S} \cdot 41/5\text{H}_2\text{O}$  :

20 C 48.64, H 5.91, N 9.61

Found : C 48.63, H 5.85, N 9.55

#### Example 72

IR (KBr) : 3300, 1651, 1506, 1437  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87-5.30 (50H, m), 6.66-8.73 (20H, m)

25 MASS (m/z) : 1236.29 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{70}\text{N}_9\text{NaO}_{21}\text{S} \cdot 23/3\text{H}_2\text{O}$  :

C 48.10, H 6.15, N 9.01

Found : C 48.14, H 6.03, N 8.97

30 The following compounds [Examples 73 and 74] were obtained in a manner similar to that of Example 17.

#### Example 73

IR (KBr) : 3359, 1676, 1651, 1632, 1514  $\text{cm}^{-1}$

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.87-1.0 (6H, m), 1.09 (3H, d,

$J=5.4\text{Hz}$ ), 1.2-1.6 (4H, m), 1.6-2.1 (5H, m), 2.1-2.6

35 (5H, m), 3.00 (1H, m), 3.2 (1H, m), 3.5 (1H, m), 3.6-4.6



417

(16H, m), 4.6-5.6 (8H, m), 6.70 (1H, d, J=8.2Hz), 6.77 (1H, d, J=8.2Hz), 6.87 (1H, s), 6.97 (1H, s), 7.20 (1H, m), 7.3-7.8 (6H, m), 7.8-8.4 (6H, s), 8.4-8.8 (2H, m), 8.89 (1H, s)

5      MASS (m/z) : 1292.51 (M-Na)<sup>+</sup>  
       Elemental Analysis Calcd. for C<sub>57</sub>H<sub>70</sub>N<sub>11</sub>O<sub>20</sub>S<sub>2</sub>Na·12H<sub>2</sub>O :  
                                         C 44.67, H 6.18, N 10.05  
                  Found :     C 44.89, H 6.05, N 10.02

### Example 74

10 IR (KBr) : 3359, 1668, 1650, 1631  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.4\text{Hz}$ ), 1.08 (3H, d,  
J=5.4Hz), 1.2-1.6 (6H, m), 1.6-2.0 (7H, m), 2.1-2.4  
(4H, m), 3.01 (1H, m), 3.20 (1H, m), 3.67 (1H, m),  
3.7-4.6 (16H, m), 4.6-5.6 (8H, m), 6.68 (1H, d,  
15 J=8.2Hz), 6.76 (1H, d,  $J=8.2\text{Hz}$ ), 6.85 (1H, s), 7.15  
(2H, d,  $J=8.9\text{Hz}$ ), 7.16 (1H, s), 7.2-7.8 (4H, m), 7.88  
(2H, d,  $J=8.9\text{Hz}$ ), 7.96 (4H, s), 8.56 (1H, s), 8.84 (2H,  
s)

MASS (m/z) : 1304.08 (M-Na)<sup>+</sup>  
Elemental Analysis Calcd. for C<sub>58</sub>H<sub>70</sub>N<sub>11</sub>O<sub>20</sub>S<sub>2</sub>Na·12H<sub>2</sub>O :  
C 45.10, H 6.13, N 9.98  
Found : C 45.33, H 5.89, N 9.94

The following compounds [Examples 75 to 85] were obtained according to a similar manner to that of Example 13.

25 Example 75

IR (KBr) : 1668, 1649, 1632, 1541, 1516  $\text{cm}^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, m) 0.97 (3H, d,  $J=6.7\text{Hz}$ ),  
1.0-1.2 (3H, m), 1.2-1.4 (8H, m), 1.45-1.65 (2H, m),  
1.7-2.6 (8H, m), 2.8-3.5 (3H, m), 3.46 (2H, t,  $J=6.4\text{Hz}$ ),  
3.6-4.6 (14H, m), 4.51 (2H, s), 4.7-5.4 (8H, m),  
6.65-6.85 (2H, m), 6.88 (1H, s), 6.97 (1H, s), 7.18  
(1H, s), 7.4-7.8 (3H, m), 7.50 (2H, d,  $J=8.6\text{Hz}$ ), 8.02  
(2H, d,  $J=8.6\text{Hz}$ ), 8.0-8.2 (5H, m), 8.41 (1H, s), 8.72  
(1H, s), 8.7-8.9 (1H, m), 9.35 (1H, s)  
MASS (m/z) : 1407 ( $M^+ + 23$ )

Elemental Analysis Calcd. for  $C_{61}H_{77}N_{12}NaO_{20}S_2 \cdot 7H_2O$  :

C 48.47, H 6.07, N 11.12

Found : C 48.51, H 6.01, N 11.17

Example 76

5 IR (KBr) : 1632, 1518, 1441, 1250  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.89 (3H, t,  $J=6.6Hz$ ), 0.97 (3H, d,  $J=6.7Hz$ ), 1.10 (3H, d,  $J=5.3Hz$ ), 1.1-1.5 (6H, m), 1.6-2.5 (10H, m), 2.9-3.1 (1H, m), 3.1-3.5 (2H, m), 3.6-4.6 (14H, m), 4.03 (2H, t,  $J=6.4Hz$ ), 4.7-5.1 (4H, m), 5.15-5.25 (3H, m), 5.3-5.45 (1H, m), 6.7-6.85 (2H, m), 6.87 (1H, s), 6.97 (1H, s), 7.10 (2H, d,  $J=8.9Hz$ ), 7.18 (1H, s), 7.4-7.8 (3H, m), 7.85 (2H, d,  $J=8.9Hz$ ), 8.0-8.2 (5H, m), 8.06 (1H, s), 8.72 (1H, s), 8.75-8.9 (1H, m), 9.23 (1H, s)

15 MASS (m/z) : 1333 ( $M^+-23$ )

Elemental Analysis Calcd. for  $C_{59}H_{73}N_{12}NaO_{20}S_2 \cdot 8H_2O$  :

C 47.20, H 5.97, N 11.19

Found : C 47.27, H 6.04, N 11.26

Example 77

20 IR (KBr) : 1633, 1608, 1531, 1444, 1419  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88-1.25 (6H, m), 1.49-2.50 (11H, m), 2.84-5.48 (33H, m), 6.62-6.98 (3H, m), 7.00-7.16 (2H, m), 7.10 (2H, d,  $J=8.5Hz$ ), 7.25-7.80 (7H, m), 7.85 (2H, d,  $J=8.5Hz$ ), 7.91-8.14 (6H, m), 8.65-8.89 (2H, m)

25 MASS (m/z) : 1371.69 ( $M-Na^+$ )

Elemental Analysis Calcd. for  $C_{62}H_{74}N_{11}NaO_{21}S_2 \cdot 8H_2O$  :

C 48.34, H 5.89, N 10.00

Found : C 48.39, H 5.65, N 9.95

Example 78

30 IR (KBr) : 1649, 1605, 1541, 1516, 1448  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7Hz$ ), 1.12 (3H, d,  $J=5.9Hz$ ), 1.40-2.45 (12H, m), 2.78-3.50 (7H, m), 3.64-5.34 (23H, m), 6.47 (1H, d,  $J=8.2Hz$ ), 6.83 (1H, d,  $J=8.2Hz$ ), 6.89 (1H, s), 7.00-7.50 (10H, m), 7.67 (1H, brs), 7.98-8.20 (6H, m), 8.74 (1H, d,  $J=2.5Hz$ ),

8.65-8.92 (2H, m)

MASS (m/z) : 1343.11 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>71</sub>N<sub>12</sub>NaO<sub>20</sub>S<sub>2</sub>·7H<sub>2</sub>O :

C 48.25, H 5.74, N 11.25

5 Found : C 48.32, H 5.62, N 11.24

#### Example 79

IR (KBr) : 1637, 1539, 1512, 1443 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.7Hz), 1.11 (3H, d, J=7.1Hz), 1.36 (3H, t, J=6.9Hz), 1.73-2.52 (8H, m),  
2.79-3.34 (3H, m), 4.10 (2H, q, J=7.0Hz), 3.66-4.60  
(14H, m), 4.70-5.54 (8H, m), 6.71 (1H, d, J=8.1Hz),  
6.79 (1H, dd, J=8.4 and 1.7Hz), 6.87 (1H, s), 6.98  
(1H, d, J=1.7Hz), 7.06 (2H, d, J=8.9Hz), 7.19 (1H,  
s), 7.45 (1H, d, J=8.8Hz), 7.60 (1H, m), 7.73 (2H,  
15 d, J=8.8Hz), 7.87 (2H, d, J=8.5Hz), 7.96-8.24 (8H,  
m), 8.73 (1H, brs), 8.80 (1H, d, J=7.3Hz)

MASS (m/z) : 1287.49 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>58</sub>H<sub>67</sub>N<sub>10</sub>NaO<sub>20</sub>S<sub>2</sub>·7H<sub>2</sub>O :

C 48.46, H 5.68, N 9.74

20 Found : C 48.19, H 5.69, N 9.56

#### Example 80

IR (KBr) : 1649, 1635, 1510, 1443 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.8Hz), 1.12 (3H, d, J=5.8Hz), 1.55-2.51 (11H, m), 2.76-3.64 (3H, m),  
3.25 (3H, s), 3.64-4.60 (18H, m), 4.60-5.54 (9H, m),  
6.73 (1H, d, J=8.2Hz), 6.83 (1H, d, J=8.6Hz), 6.89  
(1H, s), 7.02-7.15 (3H, m), 7.36-7.79 (3H, m), 7.73  
(2H, d, J=8.8Hz), 7.87 (2H, d, J=8.4Hz), 8.00-8.26  
(8H, m), 8.70-8.92 (2H, m)

30 MASS (m/z) : 1361.12 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>61</sub>H<sub>73</sub>N<sub>10</sub>NaO<sub>22</sub>S<sub>2</sub>·7H<sub>2</sub>O :

C 48.47, H 5.80, N 9.27

Found : C 48.63, H 5.71, N 9.19

#### Example 81

35 IR (KBr) : 1633, 1533, 1512, 1443 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.7Hz), 1.10-1.20 (3H, m), 1.56-2.50 (12H, m), 2.88-3.28 (3H, m), 3.25 (3H, s), 3.63-4.56 (18H, m), 4.70-5.50 (8H, m), 6.69 (1H, d, J=8.1Hz), 6.77 (1H, d, J=8.1Hz), 6.87 (1H, s), 6.98 (1H, s), 7.07 (2H, d, J=8.8Hz), 7.28-7.72 (3H, m), 7.73 (2H, d, J=8.7Hz), 7.87 (2H, d, J=8.4Hz), 7.94-8.20 (8H, m), 8.64-8.92 (2H, m)

MASS (m/z) : 1345.44 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>61</sub>H<sub>73</sub>N<sub>10</sub>NaO<sub>21</sub>S<sub>2</sub>·6H<sub>2</sub>O :  
C 49.59, H 5.80, N 9.48  
Found : C 49.52, H 5.68, N 9.39

#### Example 82

IR (KBr) : 1635, 1608, 1531, 1444, 1419 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.8Hz), 1.10 (3H, d, J=5.7Hz), 1.03-1.20 (5H, m), 1.50-2.55 (14H, m), 2.55-2.77 (4H, m), 2.89-3.55 (7H, m), 3.67-4.63 (14H, m), 4.68-5.50 (8H, m), 6.71 (1H, d, J=8.2Hz), 6.78 (1H, d, J=8.2Hz), 6.87 (1H, s), 6.97 (1H, s), 7.08 (2H, d, J=8.7Hz), 7.18 (1H, s), 7.44 (1H, d, J=7.5Hz), 7.58 (1H, m), 7.71 (1H, m), 7.85 (2H, d, J=8.8Hz), 7.94-8.20 (5H, m), 8.72 (1H, s), 8.78 (1H, d, J=7.0Hz),

MASS (m/z) : 1332.99 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>77</sub>N<sub>12</sub>NaO<sub>19</sub>S<sub>2</sub>·7H<sub>2</sub>O :  
C 48.58, H 6.18, N 11.33  
Found : C 48.58, H 6.02, N 11.22

#### Example 83

IR (KBr) : 1633, 1535, 1512, 1443 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, t, J=7.4Hz), 0.97 (3H, d, J=7.1Hz), 1.11 (3H, d, J=5.6Hz), 1.35-1.56 (2H, m), 1.66-2.55 (10H, m), 2.90-3.38 (3H, m), 3.68-4.62 (16H, m), 4.75-5.52 (8H, m), 6.71 (1H, d, J=8.2Hz), 6.79 (1H, d, J=8.2Hz), 6.88 (1H, s), 6.99 (1H, s), 7.07 (2H, d, J=8.8Hz), 7.10-7.68 (3H, m), 7.73 (2H, d, J=8.7Hz), 7.86 (2H, d, J=8.4Hz), 8.05-8.25 (8H,

m), 8.50-8.92 (2H, m)

MASS (m/z) : 1315.58 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>71</sub>N<sub>10</sub>NaO<sub>20</sub>S<sub>2</sub>·10H<sub>2</sub>O :

C 47.43, H 6.04, N 9.22

5 Found : C 47.60, H 5.66, N 9.24

#### Example 84

IR (KBr) : 1647, 1539, 1512, 1448 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.7Hz), 1.16-1.20 (3H, m), 1.15 (3H, t, J=7.0Hz), 1.73-2.58 (8H, m),  
2.84-3.35 (3H, m), 3.49 (2H, q, J=7.0Hz), 3.66-4.62  
(18H, m), 4.74-5.50 (8H, m), 6.71 (1H, d, J=8.2Hz),  
6.79 (1H, d, J=8.3 and 1.7Hz), 6.88 (1H, brs), 6.98  
(1H, d, J=1.7Hz), 7.09 (2H, d, J=8.8 Hz), 7.19 (1H,  
brs), 7.36-7.69 (2H, m), 7.74 (2H, d, J=8.8Hz),  
15 7.87 (2H, d, J=8.5Hz), 8.02-8.24 (8H, m), 8.63-8.90  
(2H, m)

MASS (m/z) : 1331.2 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>71</sub>N<sub>10</sub>NaO<sub>21</sub>S<sub>2</sub>·8H<sub>2</sub>O :

C 48.06, H 5.85, N 9.34

20 Found : C 47.93, H 5.82, N 9.23

#### Example 85

IR (KBr) : 1633, 1537, 1513, 1443 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.8Hz), 1.11 (3H, d, J=5.8Hz) 1.74-2.52 (8H, m), 2.90-3.40 (3H, m), 3.35  
(3H, s), 3.62-4.57 (18H, m), 4.70-5.49 (8H, m), 6.70  
(1H, d, J=8.1Hz), 6.78 (1 H, d, J=8.1Hz), 6.87 (1H,  
s), 6.97 (1H, s), 7.09 (2H, d, J=8.8Hz), 7.10-7.51  
(3H, m), 7.74 (2H, d, J=8.7Hz), 7.87 (2H, d, J=8.7Hz),  
7.94-8.28 (8H, m), 8.56-8.92 (2H, m)

30 MASS (m/z) : 1317.28 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. for C<sub>59</sub>H<sub>69</sub>N<sub>10</sub>NaO<sub>21</sub>S<sub>2</sub>·9H<sub>2</sub>O :

C 47.13, H 5.83, N 9.32

Found : C 47.24, H 5.55, N 9.35

#### Example 86

35 To a solution of Starting Compound (86) (0.15 g) and

4-[4-[4-(5-methoxypentyloxy)biphenyl-4-yl]piperazin-1-yl]benzoic acid benzotriazol-1-yl-ester (0.12 g) in N,N-dimethylformamide (3 ml) was added diaminopyridine (0.024g), and the mixture was stirred for 15 hours at ambient temperature.

5 The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and dried under reduced pressure. The solid was dissolved in diluted NaHCO<sub>3</sub> aq., and subjected to column chromatography on ODS (YMC-gel ODS-AM S-50 (Trademark : prepared by Yamamura Chemical Lab.))  
10 eluting with 60% methanol aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove methanol. The residue was lyophilized to give Object Compound (86) (0.16 g).

IR (KBr) : 1666.2, 1629.6, 1228.4, 1043.3 cm<sup>-1</sup>

15 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.4Hz), 1.08 (3H, d, J=5.4Hz), 1.44-5.17 (55H, m), 6.69-8.72 (22H, m)

MASS (m/z) : 1405.4 (M+Na)

Elemental Analysis Calcd. for C<sub>64</sub>H<sub>83</sub>N<sub>10</sub>NaO<sub>21</sub>S·7.5H<sub>2</sub>O :

C 50.62, H 6.50, N 9.32

20 Found : C 50.52, H 6.42, N 9.16

The following compounds [Examples 87 to 105] were obtained in a manner similar to that of Example 86.

Example 87

IR (KBr) : 1668.1, 1629.6, 1230.4 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.6Hz), 1.07 (3H, d, J=5.7Hz), 1.24-5.50 (59H, m), 6.68-8.80 (18H, m)

MASS (m/z) : 1327.5 (M-Na)

Elemental Analysis Calcd. for C<sub>60</sub>H<sub>83</sub>N<sub>10</sub>NaO<sub>20</sub>S·6.5H<sub>2</sub>O :

C 49.07, H 6.59, N 9.54

30 Found : C 49.05, H 6.64, N 9.44

Example 88

IR (KBr) : 1666.2, 1631.5, 1240.0 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.07 (3H, d, J=5.9Hz), 1.40-5.40 (52H, m), 6.69-8.71 (19H, m)

35 MASS (m/z) : 1249.3 (M-Na)

Elemental Analysis Calcd. for  $C_{58}H_{77}N_{10}NaO_{19}S \cdot 8H_2O$  :  
C 49.15, H 6.61, N 9.88  
Found : C 48.96, H 6.49, N 9.79

Example 89

5 IR (KBr) : 1668.1, 1631.5, 1238.1  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.82-5.38 (69H, m), 6.69-8.40 (14H, m)  
MASS (m/z) : 1265.6, 1243.5 (M-Na)  
Elemental Analysis Calcd. for  $C_{57}H_{83}N_{10}NaO_{19}S \cdot 7H_2O$  :  
10 C 49.13, H 7.02, N 10.05  
Found : C 49.19, H 7.02, N 10.00

Example 90

IR (KBr) : 1664.3, 1629.6, 1232.3  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7Hz$ ), 1.07 (3H, d,  $J=5.6Hz$ ), 1.16-5.20 (53H, m), 6.70-8.30 (18H, m)  
15 MASS (m/z) : 1265.4 (M-Na)  
Elemental Analysis Calcd. for  $C_{58}H_{77}N_{10}NaO_{20}S \cdot 8.5H_2O$  :  
C 48.29, H 6.57, N 9.71  
Found : C 48.04, H 6.21, N 9.60

20 Example 91

IR (KBr) : 1666.2, 1631.5, 1232.3, 1045.2  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7Hz$ ), 1.07 (3H, d,  $J=5.8Hz$ ), 1.30-5.40 (53H, m), 6.69-8.71 (18H, m)  
MASS (m/z) : 1296.3 (M+Na)  
25 Elemental Analysis Calcd. for  $C_{58}H_{77}N_{10}NaO_{19}S \cdot 8H_2O$  :  
C 49.15, H 6.61, N 9.88  
Found : C 49.14, H 6.53, N 9.90

Example 92

IR (KBr) : 3330.5, 1666.2, 1631.5, 1255.4  $cm^{-1}$   
30 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.94-5.26 (68H, m), 6.66-8.26 (11H, m)  
MASS (m/z) : 1319.35 (M-Na)  
Elemental Analysis Calcd. for  $C_{57}H_{79}N_{10}NaO_{22}S_2 \cdot 4.5H_2O$  :  
C 48.06, H 6.23, N 9.83  
35 Found : C 48.10, H 6.26, N 9.72

Example 93IR (KBr) : 1660.4, 1631.5, 1442.5, 1249.6  $\text{cm}^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.88-1.45 (11H, m), 1.60-3.40 (18H, m), 3.75-5.30 (22H, m), 6.72-9.00 (20H, m)

5 MASS (m/z) : 1334.69 (M-Na)

Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{71}\text{N}_{10}\text{NaO}_{22}\text{S}_2 \cdot 6\text{H}_2\text{O}$  :

C 48.29, H 5.70, N 9.54

Found : C 48.40, H 5.62, N 9.44

Example 9410 IR (KBr) : 1666.2, 1631.5, 1515.8, 1257.4, 1178.3  $\text{cm}^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.94-5.25 (51H, m), 6.67-8.84 (16H, m)

MASS (m/z) : 1341.55 (M-Na)

Elemental Analysis Calcd. for  $\text{C}_{59}\text{H}_{77}\text{N}_{10}\text{NaO}_{22}\text{S}_2 \cdot 6\text{H}_2\text{O}$  :

15 C 48.09, H 6.09, N 9.51

Found : C 47.98, H 6.01, N 9.49

Example 95IR (KBr) : 1666.2, 1629.6, 1257.4, 1178.3  $\text{cm}^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.94-5.16 (55H, m), 6.41-8.84 (18H, m)

20 MASS (m/z) : 1289.3 (M-Na)

Elemental Analysis Calcd. for  $\text{C}_{55}\text{H}_{73}\text{N}_{10}\text{NaO}_{22}\text{S}_2 \cdot 7\text{H}_2\text{O}$  :

C 45.89, H 6.09, N 9.73

Found : C 45.67, H 5.91, N 9.74

Example 9625 IR (KBr) : 1666.2, 1633.4, 1249.6  $\text{cm}^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96-5.20 (47H, m), 6.72-9.29 (24H, m)

MASS (m/z) : 1351.41 (M-Na)

Elemental Analysis Calcd. for  $\text{C}_{63}\text{H}_{71}\text{N}_{10}\text{NaO}_{22}\text{S} \cdot 8.5\text{H}_2\text{O}$  :

C 49.51, H 5.80, N 9.16

30 Found : C 49.64, H 5.49, N 9.13

Example 97

IR (KBr) : 1666.2, 1631.5, 1515.8, 1257.4,

1178.3  $\text{cm}^{-1}$ NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.94-5.24 (55H, m), 6.72-8.84 (20H,

35 m)



MASS (m/z) : 1363.41 (M-Na)

Elemental Analysis Calcd. for  $C_{61}H_{75}N_{10}NaO_{22}S_2 \cdot 7H_2O$  :

C 48.41, H 5.93, N 9.25

Found : C 48.45, H 5.80, N 9.14

5 Example 98

IR (KBr) : 3355.5, 2935.1, 2873.4, 1633.4, 1521.6,  
1438.6, 1255.4  $cm^{-1}$

10 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.85-1.05 (m, 6H), 1.10 (d, 3H,  
J=5.8Hz), 1.25-1.60 (m, 4H), 1.60-2.60 (m, 9H),  
2.80-3.10 (m, 1H), 3.10-3.60 (m, 2H), 3.60-4.60 (m,  
16H), 4.60-5.60 (m, 9H), 6.71 (d, 1H, J=8.2Hz), 6.81  
(d, 1H, J=8.2Hz), 6.89 (s, 1H), 7.05 (s, 1H), 7.08  
(d, 2H, J=8.9Hz), 7.15-7.30 (m, 1H), 7.30-7.55 (m,  
2H), 7.55-7.70 (m, 1H), 7.80 (d, 2H, J=8.3Hz), 7.91  
15 (d, 2H, J=8.9Hz), 7.96 (d, 2H, J=8.3Hz), 8.00-8.20  
(m, 1H), 8.38 (s, 1H), 8.65 (d, 1H, J=6.8Hz),  
8.75-9.00 (m, 1H)

MASS (m/z) : 1268.40 (M-Na)

Elemental Analysis Calcd. for  $C_{56}H_{70}N_9NaO_{21}S_2 \cdot 8H_2O$  :

20 C 46.82, H 6.03, N 8.78

Found : C 47.11, H 5.84, N 8.82

Example 99

IR (KBr) : 3396.0, 2933.2, 2871.5, 1648.8, 1631.5,  
1538.9, 1515.8, 1456.0, 1438.6, 1253.5  $cm^{-1}$

25 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.75-0.90 (m, 3H), 0.96 (d, 3H,  
J=6.7Hz), 1.11 (d, 3H, J=5.8Hz), 1.10-1.60 (m, 6H),  
1.60-2.60 (m, 9H), 2.80-3.10 (m, 1H), 3.10-3.60 (m,  
2H), 3.60-4.65 (m, 16H), 4.65-5.60 (m, 9H), 6.73 (d,  
1H, J=8.2Hz), 6.82 (d, 1H, J=8.2Hz), 6.89 (s, 1H),  
30 7.05 (s, 1H), 7.07 (d, 2H, J=8.9Hz), 7.15-7.30 (m,  
1H), 7.30-7.55 (m, 2H), 7.55-7.75 (m, 1H), 7.80 (d,  
2H, J=8.3Hz), 7.91 (d, 2H, J=8.9Hz), 7.96 (d, 2H,  
J=8.3Hz), 8.00-8.20 (m, 1H), 8.38 (s, 1H), 8.65 (d,  
1H, J=6.8Hz), 8.75-9.00 (m, 1H)

35 MASS (m/z) : 1282.09 (M-Na)

Elemental Analysis Calcd. for  $C_{57}H_{72}N_9NaO_{21}S_2 \cdot 7H_2O$  :

C 47.79, H 6.05, N 8.80

Found : C 47.89, H 5.96, N 8.77

Example 100

5 IR (KBr) : 3430.7, 2931.3, 2858.0, 1668.1, 1648.0,  
1631.5, 1515.8, 1456.0, 1438.6, 1255.4  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.75-0.90 (m, 3H), 0.96 (d, 3H,  
J=6.7Hz), 1.11(d, 3H, J=5.6Hz), 1.10-1.55 (m, 8H),  
1.60-2.60 (m, 9H), 2.80-3.10 (m, 1H), 3.10-3.60 (m,  
10 2H), 3.60-4.65 (m, 16H), 4.65-5.40 (m, 9H), 6.74 (d,  
1H, J=8.2Hz), 6.83 (d, 1H, J=8.2Hz), 6.89 (s, 1H),  
7.05 (s, 1H), 7.08 (d, 2H, J=8.8Hz), 7.20(s, 1H),  
7.30-7.55 (m, 2H), 7.60-7.75 (m, 1H), 7.80 (d, 2H,  
J=8.2Hz), 7.92 (d, 2H, J=8.8Hz), 7.96 (d, 2H,  
15 J=8.2Hz), 8.07 (d, 1H, J=7.0Hz), 8.38 (s, 1H), 8.66  
(d, 1H, J=6.8Hz), 8.85 (s, 1H)

MASS (m/z) : 1296.16 (M-Na)

Elemental Analysis Calcd. for  $C_{58}H_{74}N_9NaO_{21}S_2 \cdot 6H_2O$  :

C 48.77, H 6.07, N 8.82

20 Found : C 48.61, H 6.06, N 8.78

Example 101

IR (KBr) : 3425.0, 2969.8, 2937.1, 2881.1, 1633.4,  
1517.7, 1438.6, 1247.7  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.80-1.10 (m, 6H), 1.10 (d, 3H,  
25 J=5.7Hz), 1.60-2.60 (m, 10H), 2.85-3.10 (m, 1H),  
3.10-3.60 (m, 2H), 3.60-4.60 (m, 16H), 4.65-5.50 (m,  
8H), 6.71 (d, 1H, J=8.1Hz), 6.79 (d, 1H, J=8.1Hz),  
6.88 (s, 1H), 6.98 (s, 1H), 7.06 (d, 2H, J=8.8Hz),  
7.20 (m, 1H), 7.30-8.20 (m, 12H), 7.70 (d, 2H,  
30 J=8.8Hz), 8.48 (s, 1H), 8.60-8.85 (m, 2H)

MASS (m/z) : 1300.35 (M-Na)

Elemental Analysis Calcd. for  $C_{60}H_{70}N_9NaO_{20}S_2 \cdot 7H_2O$  :

C 49.68, H 5.84, N 8.69

Found : C 49.59, H 5.49, N 8.68

Example 102

IR (KBr) : 3349.7, 2937.1, 2871.5, 1633.4, 1519.6,  
1438.6, 1255.4  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.70-1.05 (m, 6H), 1.08 (d, 3H,  
J=5.9Hz), 1.20-1.55 (m, 4H), 1.60-2.60 (m, 10H),  
2.80-3.10 (m, 1H), 3.10-3.60 (m, 2H), 3.60-4.60 (m,  
16H), 4.60-5.50 (m, 8H), 6.70 (d, 1H, J=8.1Hz), 6.77  
(d, 1H, J=8.1Hz), 6.86 (s, 1H), 6.96 (s, 1H), 7.07  
(d, 2H, J=8.9Hz), 7.20 (m, 1H), 7.30-7.50 (m, 1H),  
10 7.50-7.80 (m, 2H), 7.79 (d, 2H, J=8.4Hz), 7.90 (d,  
2H, J=8.9Hz), 7.96 (d, 2H, J=8.4Hz), 8.00-8.20 (m,  
1H), 8.37 (s, 1H), 8.50-8.80 (m, 2H)

MASS (m/z) : 1252.57 (M-Na)

Elemental Analysis Calcd. for  $\text{C}_{56}\text{H}_{70}\text{N}_9\text{NaO}_{20}\text{S}_2 \cdot 7\text{H}_2\text{O}$  :

15 C 47.96, H 6.04, N 8.99  
Found : C 47.78, H 5.87, N 8.87

Example 103

IR (KBr) : 3432.7, 2935.1, 2869.6, 1633.4, 1535.1,  
1438.6, 1251.6  $\text{cm}^{-1}$

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.75-0.95 (m, 3H), 0.97 (d, 3H,  
J=6.8Hz), 1.10 (d, 3H, J=5.9Hz), 1.20-1.55 (m, 6H),  
1.60-2.60 (m, 10H), 2.80-3.10 (m, 1H), 3.10-3.60 (m,  
2H), 3.60-4.60 (m, 16H), 4.65-5.50 (m, 8H), 6.71 (d,  
1H, J=8.2Hz), 6.78 (d, 1H, J=8.2Hz), 6.87 (s, 1H),  
25 6.97 (s, 1H), 7.04 (d, 2H, J=8.7Hz), 7.20 (m, 1H),  
7.30-7.90 (m, 3H), 7.67 (d, 2H, J=8.7Hz), 8.01 (s,  
4H), 8.05-8.20 (m, 1H), 8.26 (s, 1H), 8.60-8.90 (m,  
2H)

MASS (m/z) : 1266.27 (M-Na)

30 Elemental Analysis Calcd. for  $\text{C}_{57}\text{H}_{72}\text{N}_9\text{NaO}_{20}\text{S}_2 \cdot 6\text{H}_2\text{O}$  :

C 48.96, H 6.05, N 9.01  
Found : C 49.07, H 5.97, N 8.94

Example 104

IR (KBr) : 3353.6, 2931.3, 2861.8, 1631.5, 1519.6,  
35 1438.6, 1253.5  $\text{cm}^{-1}$

NMR (DMSO-d<sub>6</sub>, δ) : 0.70-0.95 (m, 3H), 0.97 (d, 3H, J=6.8Hz), 1.10 (d, 3H, J=6.0Hz), 1.20-1.60 (m, 6H), 1.60-2.60 (m, 10H), 2.80-3.10 (m, 1H), 3.10-3.60 (m, 2H), 3.60-4.65 (m, 16H), 4.70-5.50 (m, 8H), 6.71 (d, 1H, J=8.1Hz), 6.79 (d, 1H, J=8.1Hz), 6.88 (s, 1H), 6.98 (s, 1H), 7.08 (d, 2H, J=8.9Hz), 7.21 (m, 1H), 7.44 (d, 1H, J=7.4Hz), 7.50-7.80 (m, 2H), 7.80 (d, 2H, J=8.4Hz), 7.91 (d, 2H, J=8.9Hz), 7.97 (d, 2H, J=8.4Hz), 8.12 (d, 1H, J=8.1Hz), 8.37 (s, 1H), 8.60-8.80 (m, 1H), 8.72 (s, 1H)

MASS (m/z) : 1266.27 (M-Na)

Elemental Analysis Calcd. for C<sub>57</sub>H<sub>72</sub>N<sub>9</sub>NaO<sub>20</sub>S<sub>2</sub>·6H<sub>2</sub>O :

C 48.96, H 6.05, N 9.01

Found : C 48.75, H 5.98, N 8.91

Example 105

IR (KBr) : 1666.2, 1629.6, 1240.0, 1047.2 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.6Hz), 1.07 (3H, d, J=5.8Hz), 1.60-5.40 (47H, m), 6.68-8.80 (18H, m)

MASS (m/z) : 1231.3 (M+1)

Elemental Analysis Calcd. for C<sub>55</sub>H<sub>71</sub>N<sub>10</sub>NaO<sub>19</sub>S·8H<sub>2</sub>O :

C 48.03, H 6.38, N 10.18

Found : C 47.84, H 6.46, N 10.12

Example 106

A solution of Starting Compound (106) (200 mg) in N,N-dimethylformamide (4 ml) was treated with 4-[5-[4-[4-[2-(2-methoxyethoxy)ethoxy]phenyl]phenyl]-1,3,4-thiadiazol-2-yl]benzoic acid benzotrizol-1-yl ester (144 mg) and diisopropylethylamine (58 μl), and the mixture was stirred for 19 hours at room temperature. Ethyl acetate was added to the reaction mixture and the resulting precipitate was collected by filtration, washed thoroughly with ethyl acetate and diisopropyl ether and dried. The powder was dissolved in saturated aqueous sodium hydrogen carbonate solution, filtered and purified by ODS column chromatography (YMC-gel ODS-AM S-50) eluting with 17-18% aqueous acetonitrile.

Product-containing fractions were pooled, evaporated to remove acetonitrile, and lyophilized to give Object Compound (106) (225 mg) as an amorphous pale yellow powder.

IR (KBr) : 1659, 1633, 1533, 1510, 1444  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7\text{Hz}$ ), 1.10 (3H, d,  $J=5.6\text{Hz}$ ), 1.76-2.47 (8H, m), 2.83-3.32 (3H, m), 3.26 (3H, s), 3.40-4.60 (22H, m), 4.70-5.54 (8H, m), 6.69 (1H, d,  $J=8.2\text{ Hz}$ ), 6.77 (1H, d,  $J=8.2\text{Hz}$ ), 6.87 (1H, brs), 6.98 (1H, s), 7.09 (2H, d,  $J=8.8\text{Hz}$ ), 7.34-7.55 (3H, m), 7.74 (2H, d,  $J=8.7\text{Hz}$ ), 7.87 (2H, d,  $J=8.5\text{Hz}$ ), 8.00-8.20 (8H, m), 8.66-8.92 (2H, m)

MASS (m/z) : 1361.4 (M- $\text{Na}^+$ )

Elemental Analysis Calcd. for  $\text{C}_{61}\text{H}_{73}\text{N}_{10}\text{NaO}_{22}\text{S}_2 \cdot 10\text{H}_2\text{O}$  :

C 46.80, H 5.99, N 8.95

15 Found : C 46.93, H 5.80, N 8.89

The following compounds [Examples 107 to 132] were obtained in a manner similar to that of Example 106.

Example 107

IR (KBr) : 3367, 2925, 1668, 1631, 1538, 1511, 1450, 1265, 1230, 1085, 1047  $\text{cm}^{-1}$

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.07 (3H, d,  $J=5.9\text{Hz}$ ), 1.2-1.6 (5H, m), 1.6-2.1 (10H, m), 2.1-2.5 (8H, m), 2.63 (4H, m), 2.79 (2H, m), 2.98 (2H, m), 3.06 (4H, m), 3.20 (1H, m), 3.71 (2H, m), 3.8-4.6 (14H, m), 4.6-5.6 (9H, m), 6.70 (1H, d,  $J=8.2\text{ Hz}$ ), 6.78 (1H, s), 6.83 (3H, d,  $J=8.2\text{Hz}$ ), 6.94 (2H, d,  $J=8.7\text{Hz}$ ), 7.04 (3H, m), 7.2-7.7 (3H, m), 7.74 (2H, d,  $J=8.7\text{Hz}$ ), 8.07 (1H, m), 8.23 (1H, m), 8.56 (1H, m), 8.84 (1H, s)

30 MASS (m/z) : 1348.35 (M- $\text{Na}^+$ )

Elemental Analysis Calcd. For  $\text{C}_{63}\text{H}_{86}\text{N}_{11}\text{NaO}_{20}\text{S}_2 \cdot 11\text{H}_2\text{O}$  :

C 48.18, H 6.93, N 9.81

Found : C 48.19, H 6.68, N 9.71

Example 108

35 IR (KBr) : 1676, 1651, 1622, 1514  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.05-1.1 (3H, m), 1.7-2.65 (12H, m), 2.8-3.2 (7H, m), 3.60 (2H, s), 2.65-4.1 (5H, m), 4.1-4.6 (9H, m), 4.7-5.45 (8H, m), 6.65-7.85 (3H, m), 7.85-7.05 (4H, m), 7.15-7.3 (3H, m), 7.4-7.8 (3H, m), 7.52 (2H, d,  $J=8.6\text{Hz}$ ), 7.94 (2H, d,  $J=8.6\text{Hz}$ ), 8.0-8.2 (5H, m), 8.41 (1H, s), 8.72 (1H, s), 8.75-8.9 (1H, m), 9.34 (1H, s)

MASS (m/z) : 1407 ( $M^+-23$ )

Elemental Analysis Calcd. For  $C_{64}H_{75}N_{14}NaO_{19}S_2 \cdot 9H_2O$  :

C 48.24, H 5.88, N 12.30

Found : C 48.41, H 5.68, N 12.22

#### Example 109

IR (KBr) : 1649, 1632, 1541, 1514  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.10 (3H, d,  $J=5.7\text{Hz}$ ), 1.1-1.35 (5H, m), 1.35-2.5 (17H, m), 2.85-3.55 (6H, m), 3.55-4.1 (8H, m), 4.1-4.6 (9H, m), 4.7-5.45 (8H, m), 6.71 (1H, d,  $J=8.3\text{Hz}$ ), 6.78 (1H, d,  $J=8.3\text{Hz}$ ), 6.85-6.9 (1H, m), 6.9-7.0 (1H, m), 7.08 (2H, d,  $J=8.9\text{Hz}$ ), 7.1-7.25 (1H, m), 7.35-7.75 (3H, m), 7.84 (2H, d,  $J=8.9\text{Hz}$ ), 7.9-8.2 (5H, m), 8.6-8.85 (2H, m)

MASS (m/z) : 1348 ( $M^+-23$ )

#### Example 110

IR (KBr) : 1651, 1632, 1539, 1514  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.8\text{Hz}$ ), 1.10 (3H, d,  $J=5.8\text{Hz}$ ), 1.2-1.6 (5H, m), 1.6-2.75 (14H, m), 2.85-3.1 (1H, m), 3.1-3.55 (2H, m), 3.65-4.1 (5H, m), 4.1-4.6 (9H, m), 4.6-5.45 (8H, m), 6.71 (1H, d,  $J=9.0\text{Hz}$ ), 6.78 (1H, d,  $J=9.0\text{Hz}$ ), 6.85-6.95 (1H, m), 6.95-7.0 (1H, m), 7.1-7.25 (1H, m), 7.4-7.8 (3H, m), 7.46 (2H, d,  $J=8.3\text{Hz}$ ), 7.96 (2H, d,  $J=8.3\text{Hz}$ ), 8.0-8.2 (1H, m), 8.06 (2H, d,  $J=8.8\text{Hz}$ ), 8.12 (2H, d,  $J=8.8\text{Hz}$ ), 8.72 (1H, s), 8.75-8.85 (1H, m)

MASS (m/z) : 1249 ( $M^+-23$ )

Elemental Analysis Calcd. For  $C_{56}H_{69}N_{10}NaO_{19}S_2 \cdot 7H_2O$  :

C 46.86, H 6.11, N 9.76

Found : C 47.02, H 6.01, N 9.77

Example 111IR (KBr) : 1649, 1632, 1541, 1522  $\text{cm}^{-1}$ 

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.10 (3H, d,  
... $J=6.1\text{Hz}$ ), 1.1-1.65 (6H, m), 1.65-2.5 (12H, m),  
2.85-3.6 (3H, m), 3.6-4.1 (5H, m), 4.1-4.6 (10H, m),  
4.75-5.45 (8H, m), 6.71 (1H, d,  $J=8.9\text{Hz}$ ), 6.78 (1H,  
d,  $J=8.9\text{Hz}$ ), 6.85-6.9 (1H, m), 6.9-7.0 (1H, m),  
10 7.14 (2H, d,  $J=8.9\text{Hz}$ ), 7.15-7.25 (1H, m), 7.4-7.8  
(3H, m), 7.95 (2H, d,  $J=8.9\text{Hz}$ ), 8.05 (2H, d,  $J=8.9\text{Hz}$ ),  
8.1-8.2 (1H, m), 8.11 (2H, d,  $J=8.9\text{Hz}$ ), 8.72 (1H,  
s), 8.75-8.85 (1H, m)

MASS (m/z) : 1265 ( $M^+-23$ )15 Elemental Analysis Calcd. For  $\text{C}_{56}\text{H}_{69}\text{N}_{10}\text{NaO}_{20}\text{S}_2 \cdot 9\text{H}_2\text{O}$  :

C 46.34, H 6.04, N 9.65

Found : C 46.24, H 5.95, N 9.58

Example 112IR (KBr) : 1664, 1628  $\text{cm}^{-1}$ 

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.5\text{Hz}$ ), 1.05-1.2 (3H,  
m), 1.5-1.75 (6H, m), 1.75-2.5 (8H, m), 2.8-3.5 (7H,  
m), 3.6-4.1 (5H, m), 4.1-4.6 (9H, m), 4.7-5.5 (8H,  
m), 6.65-6.85 (2H, m), 6.87 (1H, s), 6.97 (1H, s),  
7.07 (2H, d,  $J=9.2\text{Hz}$ ), 7.1-7.25 (1H, m), 7.35-7.8  
25 (3H, m), 7.75 (2H, d,  $J=9.2\text{Hz}$ ), 8.0-8.2 (1H, m), 8.06  
(4H, s), 8.32 (1H, s), 8.6-8.9 (2H, m), 9.17 (1H,  
s)

MASS (m/z) : 1316 ( $M^+-23$ )Elemental Analysis Calcd. For  $\text{C}_{58}\text{H}_{70}\text{N}_{13}\text{NaO}_{19}\text{S}_2 \cdot 10\text{H}_2\text{O}$  :

30 C 45.82, H 5.97, N 11.98

Found : C 45.80, H 5.74, N 11.91

Example 113IR (KBr) : 1633, 1518, 1250  $\text{cm}^{-1}$ 

NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.8-1.05 (6H, m), 1.12 (3H, d,  $J=5.4\text{Hz}$ ),  
35 1.2-1.55 (6H, m), 1.65-2.5 (9H, m), 2.9-3.5 (3H, m),

3.6-4.6 (16H, m), 4.7-5.35 (9H, m), 6.73 (1H, d, J=8.3Hz), 6.83 (1H, d, J=8.3Hz), 6.85-6.95 (1H, m), 7.0-7.25 (2H, m), 7.10 (2H, d, J=9.1Hz), 7.3-7.55 (2H, m), 7.6-7.75 (1H, m), 7.85 (2H, d, J=9.1Hz),  
5 8.0-8.2 (5H, m), 8.36 (1H, s), 8.7-8.9 (1H, m), 8.84 (1H, s), 9.24 (1H, s)

MASS (m/z) : 1349 (M<sup>+</sup>-23)

Elemental Analysis Calcd. For C<sub>59</sub>H<sub>73</sub>N<sub>12</sub>NaO<sub>21</sub>S<sub>2</sub>·8H<sub>2</sub>O :

C 46.70, H 5.91, N 11.08

10 Found : C 46.64, H 5.88, N 10.90

#### Example 114

IR (KBr) : 1612, 1497, 1446 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.7Hz), 1.11 (3H, d, J=6.1Hz), 1.6-2.5 (12H, m), 2.6-3.1 (4H, m), 3.1-3.5 (2H, m), 3.6-4.6 (16H, m), 4.6-5.45 (8H, m), 6.71 (1H, d, J=8.9Hz), 6.78 (1H, d, J=8.9Hz), 6.87 (1H, s), 6.98 (1H, d, J=1.8Hz), 7.18 (3H, d, J=8.9Hz), 7.2-7.35 (5H, m), 7.4-7.8 (3H, m), 7.97 (2H, d, J=8.9Hz), 8.0-8.2 (1H, m), 8.09 (2H, d, J=8.4Hz),  
15 8.20 (2H, d, J=8.4Hz), 8.72 (1H, s), 8.75-8.9 (1H, m)  
20 m)

MASS (m/z) : 1310 (M<sup>+</sup>-23)

Elemental Analysis Calcd. For C<sub>61</sub>H<sub>72</sub>N<sub>11</sub>NaO<sub>20</sub>S·9H<sub>2</sub>O :

C 48.67, H 6.06, N 10.30

25 Found : C 48.67, H 5.89, N 10.15

#### Example 115

IR (KBr) : 1672, 1628, 1605, 1531, 1444 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.5Hz), 1.10 (3H, d, J=5.9Hz), 1.6-2.5 (12H, m), 2.6-3.1 (4H, m), 3.1-3.5 (2H, m), 3.6-4.6 (16H, m), 4.7-5.45 (8H, m), 6.71 (1H, d, J=8.1Hz), 6.78 (1H, d, J=8.1Hz), 6.8-6.9 (1H, m), 6.9-7.0 (1H, m), 7.18 (3H, d, J=9.2Hz), 7.2-7.35 (5H, m), 7.35-7.8 (3H, m), 7.87 (2H, d, J=9.2Hz), 8.0-8.2 (5H, m), 8.72 (1H, s), 8.75-8.85 (1H, m)

35 MASS (m/z) : 1326 (M<sup>+</sup>-23)



Elemental Analysis Calcd. For  $C_{61}H_{72}N_{11}NaO_{19}S_2 \cdot 9H_2O$  :

C 48.44, H 6.00, N 10.19

Found : C 48.54, H 5.91, N 10.15

Example 116

5 IR (KBr) : 1676, 1649, 1541, 1514, 1255  $cm^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7Hz$ ), 1.10 (3H, d,  
J=5.6Hz), 1.2-2.5 (18H, m), 2.9-3.1 (1H, m), 2.9-3.6  
(2H, m), 3.65-4.1 (5H, m), 4.1-4.6 (10H, m),  
4.7-5.45 (8H, m), 6.72 (1H, d,  $J=9.3Hz$ ), 6.78 (1H,  
10 d,  $J=9.3Hz$ ), 6.85-6.95 (1H, m), 6.95-7.0 (1H, m),  
7.1-7.25 (1H, m), 7.18 (2H, d,  $J=8.9Hz$ ), 7.4-7.8 (3H,  
m), 8.0-8.15 (5H, m), 8.21 (2H, d,  $J=8.6Hz$ ), 8.72  
(1H, s), 8.75-8.95 (1H, m)

MASS (m/z) : 1249 ( $M^+-23$ )

15 Elemental Analysis Calcd. For  $C_{56}H_{69}N_{10}NaO_{21}S \cdot 9H_2O$  :

C 46.86, H 6.11, N 9.76

Found : C 47.13, H 5.98, N 9.79

Example 117

IR (KBr) : 1659, 1628  $cm^{-1}$   
20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.8Hz$ ), 1.09 (3H, d,  
J=6.0Hz), 1.2-1.6 (5H, m), 1.6-2.7 (14H, m), 2.8-3.6  
(3H, m), 3.6-4.1 (5H, m), 4.1-4.6 (9H, m), 4.6-5.4  
(8H, m), 6.7-7.0 (4H, m), 7.1-7.2 (1H, m), 7.4-7.8  
(3H, m), 7.49 (2H, d,  $J=7.2Hz$ ), 8.05-8.2 (5H, m),  
25 8.21 (2H, d,  $J=8.4Hz$ ), 8.70 (1H, s), 8.8-8.9 (1H,  
m)

MASS (m/z) : 1233 ( $M^+-23$ )

Elemental Analysis Calcd. For  $C_{56}H_{69}N_{10}NaO_{20}S \cdot 8H_2O$  :

C 48.00, H 6.11, N 9.99

30 Found : C 47.81, H 6.04, N 9.93

Example 118

IR (KBr) : 1664, 1635, 1605, 1531, 1510, 1444  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.1Hz$ ), 1.11 (3H, d,  
J=6.0Hz), 1.07-1.37 (5H, m), 1.50-2.44 (14H, m),  
35 2.56-3.50 (11H, m), 3.65-4.60 (14H, m), 4.73-5.44

(8H, m), 6.71 (1H, d, J=8.2Hz), 6.79 (1H, d, J=8.2Hz),  
6.87 (1H, s), 6.97 (1H, s), 7.05 (2H, d, J=8.9Hz),  
7.18 (1H, s), 7.35-7.77 (2H, m), 7.44 (1H, d,  
J=9.4Hz), 7.66 (2H, d, J=8.8Hz), 7.85 (2H, d,  
J=8.5Hz), 7.95-8.21 (7H, m), 8.72 (1H, s), 8.80 (1H,  
d, J=7.5Hz)

MASS (m/z) : 1409.4 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>66</sub>H<sub>81</sub>N<sub>12</sub>NaO<sub>19</sub>S<sub>2</sub>·7H<sub>2</sub>O :

C 50.83, H 6.14, N 10.78

Found : C 51.17, H 6.03, N 10.42

#### Example 119

IR (KBr) : 1659, 1633, 1531, 1508, 1443 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.6Hz), 1.00 (3H, t,  
J=7.4Hz), 1.10 (3H, d, J=5.6Hz), 1.66-2.56 (10H, m),  
2.91-3.36 (3H, m), 3.65-4.60 (14H, m), 4.00 (2H, d,  
J=6.4Hz), 4.72-5.52 (8H, m), 6.70 (1H, d, J=8.1Hz),  
6.77 (1H, d, J=8.1Hz), 6.87 (1H, s), 6.98 (1H, s),  
7.07 (2H, d, J=8.9Hz), 7.34-7.82 (3H, m), 7.73 (2H,  
d, J=8.8Hz), 7.86 (2H, d, J=8.5Hz), 8.04-8.22 (8H,  
m), 8.74-8.92 (2H, m)

MASS (m/z) : 1301.2 (M-Na)<sup>+</sup>

Elemental Analysis Calcd. For C<sub>59</sub>H<sub>69</sub>N<sub>10</sub>NaO<sub>20</sub>S<sub>2</sub>·10H<sub>2</sub>O :

C 47.07, H 5.96, N 9.30

Found : C 46.90, H 5.72, N 9.22

#### Example 120

IR (KBr) : 1659, 1635, 1533, 1510, 1444 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.1Hz), 1.11 (3H, d,  
J=5.8Hz), 1.18 (6H, d, J=6.1Hz), 1.74-2.69 (10H, m),  
2.80-3.52 (3H, m), 3.59-4.59 (18H, m), 4.72-5.49 (8H,  
m), 6.71 (1H, d, J=8.1Hz), 6.79 (1H, dd, J=8.1 and  
1.6Hz), 6.87 (1H, s), 6.98 (1H, d, J=1.6Hz) 7.07 (2H,  
d, J=9.0Hz), 7.18 (1H, s), 7.33-7.72 (3H, m), 7.68  
(2H, d, J=8.8Hz), 7.85 (2H, d, J=8.5Hz), 7.96-8.25  
(7H, m), 8.72 (1H, s), 8.80 (1H, d, J=7.5Hz)

MASS (m/z) : 1356.3 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For  $C_{62}H_{74}N_{11}NaO_{20}S_2 \cdot 9H_2O$  :

C 48.28, H 6.01, N 9.99

Found : C 48.54, H 5.94, N 9.95

Example 121

5 IR (KBr) : 1659, 1635, 1606, 1529, 1518, 1444, 1419  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.90 (6H, s) 0.97 (3H, d,  $J=6.7Hz$ ),  
1.10 (3H, d,  $J=5.8Hz$ ), 1.03-2.66 (21H, m), 2.66-  
3.54 (8H, m), 3.65-4.58 (14H, m), 4.68-5.43 (8H, m),  
6.71 (1H, d,  $J=8.1Hz$ ), 6.79 (1H, dd,  $J=8.1$  and  $1.6Hz$ ),  
10 6.87 (1H, s), 6.98 (1H, d,  $J=1.6Hz$ ) 7.11 (2H, d,  
 $J=8.6Hz$ ), 7.18 (1H, s), 7.44 (1H, d,  $J=9.0Hz$ ),  
7.48-7.77 (2H, m), 7.88 (2H, d,  $J=8.7Hz$ ), 7.95-8.20  
(5H, m), 8.72 (1H, s), 8.78 (1H, d,  $J=7.7Hz$ )  
MASS (m/z) : 1361.4 ( $M^+-1$ )

15 Elemental Analysis Calcd. For  $C_{62}H_{82}N_{12}O_{19}S_2 \cdot 10H_2O$  :  
C 48.24, H 6.66, N 10.89  
Found : C 48.22, H 6.38, N 10.79

Example 122

IR (KBr) : 1659, 1633, 1531, 1510, 1444  $cm^{-1}$   
20 NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7Hz$ ), 1.11 (3H, d,  
 $J=5.8Hz$ ), 1.10-2.68 (18H, m), 2.90-3.55 (3H, m),  
3.66-4.62 (15H, m), 4.72-5.52 (8H, m), 6.71 (1H, d,  
 $J=8.1Hz$ ), 6.79 (1H, d,  $J=8.1Hz$ ), 6.87 (1H, s), 6.98  
(1H, s), 7.07 (2H, d,  $J=8.9Hz$ ), 7.19 (1H, s), 7.45  
25 (1H, d,  $J=8.9Hz$ ), 7.47-7.77 (1H, m), 7.71 (2H, d,  
 $J=8.8Hz$ ), 7.86 (2H, d,  $J=8.5Hz$ ), 7.93-8.28 (8H, m),  
8.54-8.92 (1H, m), 8.81 (1H, d,  $J=7.7Hz$ )  
MASS (m/z) : 1341.3 ( $M-Na^+$ )

Elemental Analysis Calcd. For  $C_{62}H_{73}N_{10}NaO_{20}S_2 \cdot 8H_2O$  :  
30 C 49.33, H 5.94, N 9.28  
Found : C 49.40, H 5.87, N 9.23

Example 123

IR (KBr) : 1659, 1633, 1531, 1443  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7Hz$ ), 1.12 (3H, d,  
35  $J=6.1Hz$ ), 1.36 (3H, t,  $J=6.9Hz$ ), 1.64-2.50 (7H, m),

2.65-3.46 (3H, m),  
4.13 (2H, q, J=7.0Hz), 3.67-4.58 (14H, m), 4.70-  
5.34 (9H, m), 6.74 (1H, d, J=8.2Hz), 6.83 (1H, d,  
J=8.2Hz), 6.90 (1H, s), 6.97-7.13 (3H, m), 7.19 (1H,  
5 s), 7.33 (1H, s), 7.44 (2H, m), 7.70 (1H, brs), 7.73  
(2H, d, J=8.8Hz), 7.87 (2H, d, J=8.5Hz), 8.00-8.22  
(6H, m), 8.80 (1H, d, J=6.9Hz), 8.84 (1H, s)

MASS (m/z) : 1303.3 (M-Na<sup>+</sup>)

10 Elemental Analysis Calcd. For C<sub>58</sub>H<sub>67</sub>N<sub>10</sub>NaO<sub>21</sub>S<sub>2</sub>·10H<sub>2</sub>O :  
C 46.21, H 5.82, N 9.29  
Found : C 46.47, H 5.65, N 9.29

Example 124

IR (KBr) : 1633, 1608, 1531, 1444, 1419 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.12 (3H, d,  
15 J=5.5Hz), 1.05-1.36 (5H, m), 1.47-2.50 (13H, m),  
2.58-3.46 (11H, m), 3.64-4.60 (14H, m), 4.70-5.34  
(9H, m), 6.74 (1H, d, J=8.2Hz), 6.83 (1H, d, J=8.2Hz),  
6.89 (1H, s), 7.08 (2H, d, J=8.7Hz), 7.01-7.25 (2H,  
m), 7.35-7.74 (3H, m), 7.86 (2H, d, J=8.8Hz),  
20 7.98-8.26 (5H, m), 8.53-8.86 (1H, m), 8.85 (1H, s)

MASS (m/z) : 1349.05 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>60</sub>H<sub>77</sub>N<sub>12</sub>NaO<sub>20</sub>S<sub>2</sub>·6H<sub>2</sub>O :  
C 48.64, H 6.05, N 11.34  
Found : C 48.38, H 6.09, N 11.15

25 Example 125

IR (KBr) : 1658, 1633, 1606, 1531, 1444, 1419 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.90 (3H, d, J=6.7Hz), 0.97 (3H, d,  
J=6.6Hz), 1.10 (3H, d, J=5.9Hz), 1.31-2.51 (18H, m),  
2.51-2.70 (4H, m), 2.88-3.46 (7H, m), 3.55-4.59 (14H,  
30 m), 4.69-5.56 (8H, m), 6.70 (1H, d, J=8.1Hz), 6.77  
(1H, d, J=8.1Hz), 6.86 (1H, s), 6.97 (1H, s) 7.08  
(2H, d, J=8.7Hz), 7.09-7.78 (3H, m), 7.86 (2H, d,  
J=8.7Hz), 7.96-8.18 (6H, m), 8.63-8.92 (1H, s), 8.78  
(1H, d, J=6.9Hz)

35 MASS (m/z) : 1347.3 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For  $C_{61}H_{79}N_{12}NaO_{19}S_2 \cdot 11H_2O$  :

C 46.68, H 6.49, N 10.71

Found : C 46.67, H 6.19, N 10.64

Example 126

5 IR (KBr) : 1658, 1633, 1606, 1531, 1518, 1444, 1417  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.86 (3H, d,  $J=6.4Hz$ ), 0.87-1.44 (2H,

m), 0.97 (3H, d,  $J=6.7Hz$ ), 1.10 (3H, d,  $J=5.9Hz$ ),  
1.60-2.55 (16H, m), 2.55-2.73 (4H, m), 2.96-3.54 (7H,  
m), 3.65-4.60 (14H, m), 4.70-5.28 (8H, m), 6.71 (1H,  
10 d,  $J=8.3Hz$ ), 6.79 (1H, dd,  $J=8.3$  and  $1.7Hz$ ), 6.87  
(1H, s), 6.98 (1H, d,  $J=1.7Hz$ ), 7.07 (2H, d,  $J=9.0Hz$ ),  
7.18 (1H, s), 7.44 (1H, d,  $J=8.4Hz$ ), 7.50-7.78 (2H,  
m), 7.85 (2H, d,  $J=8.9Hz$ ), 7.95-8.24 (5H, m), 8.72  
(1H, s), 8.79 (1H, d,  $J=7.1Hz$ )

15 MASS (m/z) : 1347.3 (M- $Na^+$ )

Elemental Analysis Calcd. For  $C_{61}H_{79}N_{12}NaO_{19}S_2 \cdot 11H_2O$  :

C 46.68, H 6.49, N 10.71

Found : C 46.77, H 6.20, N 10.65

Example 127

20 IR (KBr) : 1633, 1533, 1516, 1443,  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7Hz$ ), 1.10 (3H, d,

$J=5.6Hz$ ), 1.18 (3H, t,  $J=7.0Hz$ ), 1.73-2.52 (8H, m),  
2.86-3.38 (3H, m), 3.52 (2H, q,  $J=7.0Hz$ ), 3.63-4.60  
(16H, m), 4.53 (2H, s), 4.71-5.53 (6H, m), 6.68 (1H,  
25 d,  $J=8.0Hz$ ), 6.76 (1H, d,  $J=7.8Hz$ ), 6.87 (1H, s),  
6.98 (1H, s), 7.28-7.83 (3H, m), 7.47 (2H, d,  
 $J=8.5Hz$ ), 7.77 (2H, d,  $J=8.2Hz$ ), 7.92 (2H, d,  
 $J=8.5Hz$ ), 8.00-8.25 (8H, m), 8.70-8.85 (2H, m)

MASS (m/z) : 1301.3 (M- $Na^+$ )

30 Elemental Analysis Calcd. For  $C_{59}H_{69}N_{10}NaO_{20}S_2 \cdot 9H_2O$  :

C 47.64, H 5.89, N 9.42

Found : C 47.92, H 5.84, N 9.39

Example 128

35 IR (KBr) : 1659, 1633, 1533, 1514, 1443,  $cm^{-1}$   
NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.7Hz$ ), 1.10 (3H, d,

J=5.9Hz), 1.75-2.53 (8H, m), 2.81-3.36 (3H, m), 3.28 (3H, s), 3.47-4.64 (20H, m), 4.56 (2H, s), 4.74-5.60 (6H, m), 6.69 (1H, d, J=8.3Hz), 6.77 (1H, d, J=8.3Hz), 6.87 (1H, s), 6.98 (1H, s), 7.26-7.84 (3H, m), 7.47 (2H, d, J=8.4Hz), 7.78 (2H, d, J=8.3Hz), 7.92 (2H, d, J=8.5Hz), 8.03-8.28 (8H, m), 8.74-8.90 (2H, m)

MASS (m/z) : 1331.3 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>60</sub>H<sub>71</sub>N<sub>10</sub>NaO<sub>21</sub>S<sub>2</sub>·9H<sub>2</sub>O :  
C 47.49, H 5.91, N 9.23  
Found : C 47.36, H 5.81, N 9.16

#### Example 129

IR (KBr) : 1668, 1651, 1632, 1539, 1512 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.7Hz), 1.10-1.12 (3H, m) 1.12 (3H, t, J=7.0Hz), 1.70-2.50 (10H, m), 2.80-3.30 (3H, m), 3.41 (2H, q, J=7.0Hz), 3.53 (2H, t, J=6.4Hz), 3.66-4.60 (14H, m), 4.10 (2H, t, J=6.4Hz), 4.70-5.52 (8H, m), 6.71 (1H, d, J=8.1Hz), 6.79 (1H, dd, J=8.1 and 1.6Hz), 6.87 (1H, s), 6.98 (1H, d, J=1.6Hz), 7.08 (2H, d, J=8.8Hz), 7.18 (1H, s), 7.32-7.68 (3H, m), 7.73 (2H, d, J=8.8Hz), 7.87 (2H, d, J=8.5Hz), 8.04-8.24 (7H, m), 8.56-8.91 (1H, m), 8.81 (1H, d, J=7.0Hz)

MASS (m/z) : 1345.3 (M-Na<sup>+</sup>)  
Elemental Analysis Calcd. For C<sub>61</sub>H<sub>73</sub>N<sub>10</sub>NaO<sub>21</sub>S<sub>2</sub>·10H<sub>2</sub>O :  
C 47.28, H 6.05, N 9.04  
Found : C 47.44, H 5.91, N 9.02

#### Example 130

IR (KBr) : 1649, 1537, 1512 1443 cm<sup>-1</sup>  
NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.6Hz), 1.10 (3H, d, J=5.7Hz), 1.74-2.22 (10H, m), 2.80-3.30 (3H, m), 3.27 (3H, s), 3.50 (2H, t, J=6.3Hz), 3.65-4.60 (14H, m), 4.09 (2H, t, J=6.4Hz), 4.60-5.58 (8H, m), 6.70 (1H, d, J=8.1Hz), 6.77 (1H, d, J=8.1Hz), 6.87 (1H, s), 6.99 (1H, s), 7.07 (2H, d, J=8.9Hz), 7.10-7.72

(3H, m), 7.73 (2H, d, J=8.8Hz), 7.87 (2H, d, J=8.5Hz),  
8.00-8.35 (8H, m), 8.64-8.96 (2H, m)

MASS (m/z) : 1331.3 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>60</sub>H<sub>71</sub>N<sub>10</sub>NaO<sub>21</sub>S<sub>2</sub>·9H<sub>2</sub>O :

5 C 47.49, H 5.91, N 9.23

Found : C 47.39, H 5.75, N 9.16

#### Example 131

IR (KBr) : 3349.7, 1633.4, 1537.0, 1515.8, 1442.5,  
1419.4 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.8Hz), 1.10 (3H, d,  
J=5.3Hz), 1.7-2.5 (12H, m), 2.94 (3H, s),  
2.94-4.6 (21H, m), 4.7-5.4 (8H, m), 6.71 (1H,  
d, J=8Hz), 6.79 (1H, dd, J=8.4 and 1.7Hz), 6.88  
(1H, brs), 6.97 (1H, brs), 7.15 (2H, d, J=9Hz),  
15 7.17 (1H, brs), 7.45 (4H, s), 7.4-7.8 (3H, m),  
7.87 (2H, d, J=8.8Hz), 8.02 (4H, s), 8.02-8.07  
(1H, m), 8.72 (1H, s), 8.78 (1H, d, J=7.6Hz)

MASS (m/z) : 1390.23 (M-Na)

Elemental Analysis Calcd. For C<sub>62</sub>H<sub>73</sub>ClN<sub>11</sub>O<sub>20</sub>S<sub>2</sub>Na·7H<sub>2</sub>O :

20 C 48.32, H 5.69, N 10.00

Found : C 48.15, H 5.51, N 9.93

#### Example 132

IR (KBr) : 1633.4, 1535.1, 1523.5, 1442.5, 1419.4,  
1276.6, 1243.9 cm<sup>-1</sup>

25 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.8Hz), 1.12 (3H, d,  
J=6Hz), 1.7-2.5 (10H, m), 2.94 (3H, s), 2.9-5.4  
(31H, m), 6.73 (1H, d, J=8.3Hz), 6.81-6.85 (1H,  
m), 6.89 (1H, brs), 7.05 (1H, brs), 7.15 (2H,  
d, J=8.7Hz), 7.17 (1H, brs), 7.45 (4H, s),  
30 7.3-7.7 (3H, m), 7.87 (2H, d, J=8.7Hz), 8.06  
(4H, s), 8.0-8.15 (1H, m), 8.7-9.0 (2H, m)

MASS (m/z) : 1405.8 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>62</sub>H<sub>73</sub>ClN<sub>11</sub>O<sub>21</sub>S<sub>2</sub>Na·6H<sub>2</sub>O :

C 48.39, H 5.57, N 10.01

35 Found : C 48.39, H 5.52, N 9.90

Example 133

To a solution of 4-[2-[4-(4-piperidin-1-yl-butyl)oxy]phenyl]imidazo[2,1-b][1,3,4]thiadiazol-6-yl]benzoic acid (147 mg), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (WSCD·HCl) (74 mg) and 1-hydroxybenzotriazole (66 mg) in N,N-dimethylformamide (4 ml) was added diisopropylethylamine (0.5 ml). After stirring for 24 hours at ambient temperature, the Starting Compound (133) (200 mg) was added to the solution and the mixture was stirred for 8 hours at ambient temperature.

The reaction mixture was pulverized with ethyl acetate. The precipitate was collected by filtration, and dried under reduced pressure. The powder was dissolved in water, and subjected to column chromatography on ion exchange resin (DOWEX-50WX4 (Trademark : prepared by Dow Chemical)) eluting with water. The fractions containing the object compound were combined, and subjected to column chromatography on -ODS (YMC-gel·ODS-AM·S-50 (Trademark : prepared by Yamamura Chemical Lab.)) eluting with 20% acetonitrile aqueous solution. The fractions containing the object compound were combined, and evaporated under reduced pressure to remove acetonitrile. The residue was lyophilized to give Object Compound (133) (30 mg).

IR (KBr) : 3326, 2933, 1666, 1631, 1523, 1463, 1367, 1257  $\text{cm}^{-1}$

NMR (DMSO- $d_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.3-1.6 (8H, m), 1.6-2.15 (5H, m), 2.2-2.5 (10H, m), 2.97 (2H, m), 3.20 (1H, m), 3.74 (2H, m), 3.8-4.6 (14H, m), 4.6-5.4 (9H, m), 6.74 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.88 (1H, s), 7.04 (1H, s), 7.14 (2H, d,  $J=8.8\text{Hz}$ ), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.66 (1H, m), 7.88 (2H, d,  $J=8.8\text{Hz}$ ), 7.95 (4H, s), 8.07 (1H, d,  $J=7.8\text{Hz}$ ), 8.58 (1H, d,  $J=7.8\text{Hz}$ ), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1377.25 (M- $\text{Na}^+$ )



The following compounds [Examples 134 to 159] were obtained in a manner similar to that of Example 133.

Example 134

IR (KBr) : 3353, 2940, 1666, 1631, 1523, 1465, 1257  $\text{cm}^{-1}$   
5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.3-1.6 (10H, m), 1.6-2.15 (5H, m), 2.2-2.5 (10H, m), 2.97 (2H, m), 3.20 (1H, m) 3.74 (2H, m), 3.8-4.6 (14H, m), 4.6-5.4 (9H, m), 6.74 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.89 (1H, s),  
10 7.05 (1H, s), 7.14 (2H, d,  $J=8.8\text{Hz}$ ), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H, m), 7.90 (2H, d,  $J=8.8\text{Hz}$ ), 7.96 (4H, s), 8.07 (1H, d,  $J=7.8\text{Hz}$ ), 8.57 (1H, d,  $J=7.8\text{Hz}$ ), 8.85 (1H, s), 8.95 (1H, s)  
MASS (m/z) : 1391.13 (M- $\text{Na}^+$ )

15 Example 135

IR (KBr) : 3349, 2939, 1666, 1633, 1523, 1440, 1257  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.3-1.6 (12H, m), 1.6-2.15 (5H, m),  
2.2-2.5 (10H, m), 2.97 (2H, m), 3.20 (1H, m) 3.74 (2H, m), 3.8-4.6 (14H, m), 4.6-5.4 (9H, m), 6.74 (1H, d,  $J=8.2\text{Hz}$ ), 6.83 (1H, d,  $J=8.2\text{Hz}$ ), 6.89 (1H, s),  
20 7.05 (1H, s), 7.14 (2H, d,  $J=8.8\text{Hz}$ ), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H, m), 7.90 (2H, d,  $J=8.8\text{Hz}$ ), 7.96 (4H, s), 8.07 (1H, d,  $J=7.8\text{Hz}$ ), 8.60 (1H, d,  $J=7.8\text{Hz}$ ), 8.85 (1H, s), 8.95 (1H, s)  
25 MASS (m/z) : 1405.31 (M- $\text{Na}^+$ )

Elemental Analysis Calcd. For  $\text{C}_{63}\text{H}_{81}\text{N}_{12}\text{NaO}_{21}\text{S}_2 \cdot 8\text{H}_2\text{O}$  :

C 48.09, H 6.21, N 10.68

Found : C 48.04, H 6.15, N 10.49

30 Example 136

IR (KBr) : 3351, 2939, 1658, 1633, 1527, 1465, 1444, 1257  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.95 (3H, d,  $J=6.7\text{Hz}$ ), 1.11 (3H, d,  $J=5.7\text{Hz}$ ), 1.3-1.6 (4H, m), 1.6-2.15 (5H, m), 2.2-2.5 (10H, m), 2.97 (2H, m), 3.20 (1H, m) 3.56 (4H, t,  
35

J=4.6Hz), 3.71 (2H, m), 3.8-4.6 (14H, m), 4.6-5.4 (9H, m), 6.74 (1H, d, J=8.2Hz), 6.85 (1H, d, J=8.2Hz), 6.93 (1H, s), 7.04 (1H, s), 7.14 (2H, d, J=8.8Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H, m), 7.90 (2H, d, J=8.8Hz), 7.96 (4H, s), 8.07 (1H, d, J=7.8Hz), 8.57 (1H, d, J=7.8Hz), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1392.65 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>61</sub>H<sub>77</sub>N<sub>12</sub>NaO<sub>22</sub>S<sub>3</sub>·10H<sub>2</sub>O :

C 45.86, H 6.12, N 10.52

Found : C 45.75, H 5.83, N 10.46

#### Example 137

IR (KBr) : 3347, 2935, 1666, 1631, 1523, 1463, 1255, 1078, 1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.7Hz), 1.03 (6H, d, J=6.3Hz), 1.11 (3H, d, J=5.7Hz), 1.3-1.6 (6H, m), 1.6-2.15 (5H, m), 2.2-2.5 (6H, m), 2.71 (2H, d, J=10.2Hz), 2.97 (2H, m), 3.20 (1H, m) 3.56 (2H, m) 3.71 (2H, m), 3.8-4.6 (14H, m), 4.6-5.4 (9H, m), 6.74 (1H, d, J=8.2Hz), 6.85 (1H, d, J=8.2Hz), 6.93 (1H, s), 7.04 (1H, s), 7.14 (2H, d, J=8.8Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H, m), 7.90 (2H, d, J=8.8Hz), 7.96 (4H, s), 8.07 (1H, d, J=7.8Hz), 8.57 (1H, d, J=7.8Hz), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1420.94 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>63</sub>H<sub>81</sub>N<sub>12</sub>NaO<sub>22</sub>S<sub>2</sub>·8H<sub>2</sub>O :

C 47.60, H 6.15, N 10.57

Found : C 47.84, H 6.06, N 10.50

#### Example 138

IR (KBr) : 3347, 2937, 1666, 1631, 1521, 1465, 1257, 1074, 1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.7Hz), 1.03 (6H, d, J=6.3Hz), 1.08 (3H, d, J=5.7Hz), 1.3-1.6 (6H, m), 1.6-2.15 (5H, m), 2.2-2.5 (6H, m), 2.45 (2H, m), 2.71 (2H, d, J=10.2Hz), 2.97 (2H, m), 3.20 (1H, m) 3.56 (2H, m) 3.71 (2H, m), 3.8-4.6 (13H, m), 4.6-5.4 (8H,

m), 6.68 (1H, d, J=8.2Hz), 6.76 (1H, d, J=8.2Hz),  
6.86 (1H, s), 6.97 (1H, s), 7.14 (2H, d, J=8.9Hz),  
7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H, m), 7.90  
(2H, m), 7.96 (4H, s), 8.07 (1H, m), 8.60 (1H, m),  
8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1405.74 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>63</sub>H<sub>81</sub>N<sub>12</sub>NaO<sub>21</sub>S<sub>2</sub>·9H<sub>2</sub>O :

C 47.54, H 6.27, N 10.56

Found : C 47.68, H 6.21, N 10.50

10 Example 139

MASS (m/z) : 1435.29 (M-Na<sup>+</sup>)

Example 140

IR (KBr) : 3328, 2939, 1664, 1633, 1525, 1465, 1442, 1257,  
1047 cm<sup>-1</sup>

15 NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.7Hz), 1.10 (3H, d,  
J=5.7Hz), 1.3-1.6 (6H, m), 1.6-2.15 (5H, m), 2.2-2.5  
(6H, m), 2.5-2.7 (2H, m), 2.59 (4H, s), 2.97 (2H,  
m), 3.20 (1H, m) 3.73 (2H, m), 3.8-4.6 (14H, m),  
4.6-5.4 (9H, m), 6.69 (1H, d, J=8.2Hz), 6.80 (1H,  
20 d, J=8.2Hz), 6.88 (1H, s), 7.05 (1H, s), 7.14 (2H,  
d, J=8.8Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H,  
m), 7.90 (2H, d, J=8.8Hz), 7.96 (4H, s), 8.07 (1H, d,  
J=7.8Hz), 8.57 (1H, d, J=7.8Hz), 8.85 (1H, s), 8.95  
(1H, s)

25 MASS (m/z) : 1408.94 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>61</sub>H<sub>77</sub>N<sub>12</sub>NaO<sub>21</sub>S<sub>3</sub>·10H<sub>2</sub>O :

C 45.40, H 6.06, N 10.42

Found : C 45.49, H 5.59, N 10.26

Example 141

30 IR (KBr) : 3340, 2939, 1631, 1523, 1465, 1442, 1257,  
1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d,  
J=5.7Hz), 1.3-1.6 (4H, m), 1.6-2.15 (5H, m), 2.2-2.5  
(4H, m), 2.97 (2H, m), 3.20 (1H, m) 3.23 (3H, s),  
35 3.34 (2H, t J=6.2Hz), 3.73 (2H, m), 3.8-4.6 (14H,

m), 4.6-5.4 (9H, m), 6.69 (1H, d, J=8.2Hz), 6.76 (1H, d, J=8.2Hz), 6.88 (1H, s), 7.04 (1H, s), 7.14 (2H, d, J=8.8Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H, m), 7.90 (2H, d, J=8.8Hz), 7.95 (4H, s), 8.07 (1H, m),  
5 8.57 (1H, m), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1338.33 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>58</sub>H<sub>72</sub>N<sub>11</sub>NaO<sub>22</sub>S<sub>2</sub>·10H<sub>2</sub>O :

C 45.16, H 6.01, N 9.99

Found : C 45.39, H 5.80, N 10.02

10 Example 142

IR (KBr) : 3340, 2935, 1648, 1631, 1537, 1515, 1456, 1257,  
1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d, J=5.7Hz), 1.3-1.6 (4H, m), 1.6-2.15 (5H, m), 2.2-2.5  
15 (6H, m), 2.97 (2H, m), 3.20 (1H, m) 3.23 (3H, s),  
3.34 (2H, t J=6.2Hz), 3.74 (2H, m), 3.8-4.6 (13H, m), 4.6-5.4 (8H, m), 6.68 (1H, d, J=8.2Hz), 6.76 (1H, d, J=8.2Hz), 6.86 (1H, s), 6.97 (1H, s), 7.14 (2H, d, J=8.9Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H, m),  
20 7.90 (2H, m), 7.96 (4H, s), 8.07 (1H, m), 8.60 (1H, m), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1322.3 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>58</sub>H<sub>72</sub>N<sub>11</sub>NaO<sub>21</sub>S<sub>2</sub>·9H<sub>2</sub>O :

C 46.18, H 6.01, N 10.21

25 Found : C 45.96, H 5.86, N 10.12

Example 143

IR (KBr) : 3349, 2937, 1666, 1631, 1523, 1465, 1257,  
1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d, J=5.7Hz), 1.3-1.6 (6H, m), 1.6-2.15 (5H, m), 2.2-2.5  
30 (4H, m), 2.97 (2H, m), 3.20 (1H, m) 3.23 (3H, s),  
3.34 (2H, t J=6.2Hz), 3.73 (2H, m), 3.8-4.6 (14H, m), 4.6-5.4 (9H, m), 6.69 (1H, d, J=8.2Hz), 6.76 (1H, d, J=8.2Hz), 6.88 (1H, s), 7.04 (1H, s), 7.14 (2H, d, J=8.8Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H,  
35

m), 7.90 (2H, d, J=8.8Hz), 7.95 (4H, s), 8.07 (1H, m),  
8.57 (1H, m), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1352.48 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>59</sub>H<sub>74</sub>N<sub>11</sub>NaO<sub>22</sub>S<sub>2</sub>·12H<sub>2</sub>O :

5 C 44.50, H 6.20, N 9.67  
Found : C 44.74, H 5.71, N 9.70

Example 144

IR (KBr) : 3330, 2931, 1666, 1631, 1523, 1465, 1257,  
1047 cm<sup>-1</sup>

10 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d,  
J=5.7Hz), 1.3-1.6 (8H, m), 1.6-2.15 (5H, m), 2.2-2.5  
(4H, m), 2.97 (2H, m), 3.20 (1H, m) 3.23 (3H, s),  
3.34 (2H, t J=6.2Hz), 3.73 (2H, m), 3.8-4.6 (14H,  
m), 4.6-5.4 (9H, m), 6.69 (1H, d, J=8.2Hz), 6.76 (1H,  
15 d, J=8.2Hz), 6.88 (1H, s), 7.04 (1H, s), 7.14 (2H,  
d, J=8.8Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H,  
m), 7.90 (2H, d, J=8.8Hz), 7.95 (4H, s), 8.07 (1H, m),  
8.57 (1H, m), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1366.46 (M-Na<sup>+</sup>)

20 Elemental Analysis Calcd. For C<sub>60</sub>H<sub>76</sub>N<sub>11</sub>NaO<sub>22</sub>S<sub>2</sub>·13H<sub>2</sub>O :  
C 44.36, H 6.33, N 9.48  
Found : C 44.40, H 5.88, N 9.30

Example 145

25 IR (KBr) : 3324, 2933, 1666, 1631, 1523, 1465, 1257,  
1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d,  
J=5.7Hz), 1.3-1.6 (10H, m), 1.6-2.15 (5H, m),  
2.2-2.5 (4H, m), 2.97 (2H, m), 3.20 (1H, m) 3.23 (3H,  
30 s), 3.34 (2H, t J=6.2Hz), 3.73 (2H, m), 3.8-4.6 (14H,  
m), 4.6-5.4 (9H, m), 6.69 (1H, d, J=8.2Hz), 6.76 (1H,  
d, J=8.2Hz), 6.88 (1H, s), 7.04 (1H, s), 7.14 (2H,  
d, J=8.8Hz), 7.23 (1H, m), 7.3-7.5 (2H, m), 7.67 (1H,  
m), 7.90 (2H, d, J=8.8Hz), 7.95 (4H, s), 8.07 (1H, m),  
35 8.57 (1H, m), 8.85 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1380.30 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>61</sub>H<sub>78</sub>N<sub>11</sub>NaO<sub>22</sub>S<sub>2</sub>·10H<sub>2</sub>O :

C 46.24, H 6.23, N 9.72

Found : C 46.29, H 6.02, N 9.71

5 Example 146

IR (KBr) : 3351, 3330, 2935, 1664, 1633, 1606, 1529, 1465,  
1446, 1267, 1238 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.4Hz), 1.10 (3H, d,  
J=5.4Hz), 1.60 (6H, s), 1.7-2.1 (3H, m), 2.1-2.6 (4H,  
10 m), 2.98 (2H, m), 3.20 (1H, m) 3.4 (4H, m), 3.73 (2H,  
m), 3.8-4.6 (12H, m), 4.6-5.6 (9H, m), 6.70 (1H, d,  
J=8.2Hz), 6.81 (1H, d, J=8.2Hz), 6.89 (1H, s), 7.05  
(1H, s), 7.06 (2H, d, J=8.9Hz), 7.2-7.7 (4H, m), 7.74  
(2H, d, J=8.9Hz), 7.94 (4H, s), 8.07 (1H, m), 8.56  
15 (1H, m), 8.79 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1304.84 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>57</sub>H<sub>69</sub>N<sub>12</sub>NaO<sub>20</sub>S<sub>2</sub>·7H<sub>2</sub>O :

C 47.04, H 5.75, N 11.55

Found : C 47.32, H 5.75, N 11.67

20 Example 147

IR (KBr) : 3351, 3330, 2933, 1668, 1631, 1515, 1454, 1268,  
1236 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.4Hz), 1.11 (3H, d,  
J=5.4Hz), 1.6-2.1 (3H, m), 2.1-2.6 (4H, m), 2.98 (2H,  
25 m), 3.20 (1H, m) 3.4 (4H, m), 3.76 (6H, m), 3.8-  
4.6 (12H, m), 4.6-5.6 (9H, m), 6.70 (1H, d, J=8.2Hz),  
6.81 (1H, d, J=8.2Hz), 6.89 (1H, s), 7.05 (1H, s),  
7.06 (2H, d, J=8.9Hz), 7.2-7.7 (4H, m), 7.74 (2H,  
d, J=8.9Hz), 7.94 (4H, s), 8.07 (1H, m), 8.56 (1H,  
30 m), 8.79 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1306.85 (M-Na<sup>+</sup>)

Example 148

IR (KBr) : 3355, 2975, 2935, 1666, 1631, 1610, 1523, 1465,  
1241 cm<sup>-1</sup>

35 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d,

J=5.7Hz), 1.18 (6H, d, J=6.2Hz), 1.6-2.1 (3H, m),  
2.1-2.6 (6H, m), 2.98 (2H, m), 3.20 (1H, m) 3.4 (2H,  
m), 3.73 (4H, m), 3.8-4.6 (12H, m), 4.6-5.6 (9H, m),  
6.70 (1H, d, J=8.2Hz), 6.81 (1H, d, J=8.2Hz), 6.89  
5 (1H, s), 7.04 (1H, s), 7.11 (2H, d, J=8.9Hz), 7.2-7.7  
(4H, m), 7.78 (2H, d, J=8.9Hz), 7.95 (4H, s), 8.07  
(1H,m), 8.54 (1H, m), 8.80 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1334.95 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>58</sub>H<sub>71</sub>N<sub>12</sub>NaO<sub>21</sub>S<sub>2</sub>·10H<sub>2</sub>O :  
10 C 45.25, H 5.96, N 10.92  
Found : C 45.25, H 5.76, N 10.94

Example 149

IR (KBr) : 3355, 2971, 2933, 1668, 1648, 1631, 1610, 1535,  
1515, 1463, 1241 cm<sup>-1</sup>  
15 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d,  
J=5.7Hz), 1.18 (6H, d, J=6.2Hz), 1.6-2.1 (3H, m),  
2.1-2.6 (8H, m), 2.98 (2H, m), 3.20 (1H, m) 3.4 (2H,  
m), 3.73 (4H, m), 3.8-4.6 (11H, m), 4.6-5.6 (8H, m),  
6.70 (1H, d, J=8.2Hz), 6.81 (1H, d, J=8.2Hz), 6.89  
20 (1H, s), 6.96 (1H, s), 7.12 (2H, d, J=8.9Hz), 7.2-7.7  
(4H, m), 7.78 (2H, d, J=8.9Hz), 7.95 (4H, s), 8.12  
(1H,m), 8.56 (1H, m), 8.80 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1319.3 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>58</sub>H<sub>71</sub>N<sub>12</sub>NaO<sub>20</sub>S<sub>2</sub>·9H<sub>2</sub>O :  
25 C 46.27, H 5.96, N 11.16  
Found : C 46.03, H 5.85, N 11.02

Example 150

IR (KBr) : 3353, 2927, 1666, 1631, 1608, 1535, 1465, 1432,  
1265, 1193, 1047 cm<sup>-1</sup>  
30 NMR (DMSO-d<sub>6</sub>, δ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d,  
J=5.7Hz), 1.6-2.1 (3H, m), 2.1-2.6 (4H, m), 2.66 (4H,  
m), 2.98 (2H, m), 3.20 (1H, m), 3.73 (2H, m), 3.79  
(4H, m), 3.8-4.6 (12H, m), 4.6-5.6 (9H, m), 6.72 (1H,  
d, J=8.2Hz), 6.81 (1H, d, J=8.2Hz), 6.88 (1H, s),  
35 7.04 (1H, s), 7.11 (2H, d, J=8.9Hz), 7.2-7.7 (4H,

m), 7.77 (2H, d, J=8.9Hz), 7.94 (4H, s), 8.07 (1H, m),  
8.54 (1H, m), 8.80 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1322.96 (M-Na<sup>+</sup>)

Example 151

5 IR (KBr) : 3353, 1666, 1629, 1523, 1454, 1378, 1268,  
1238 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.9-1.4 (9H, m), 1.4-2.1 (3H, m),  
2.1-2.6 (10H, m), 2.98 (2H, m), 3.20 (1H, m), 3.4  
10 (4H, m), 3.74 (2H, m), 3.8-4.6 (12H, m), 4.6-5.6 (9H,  
m), 6.72 (1H, d, J=8.2Hz), 6.81 (1H, d, J=8.2Hz),  
6.88 (1H, s), 7.05 (1H, s), 7.09 (2H, d, J=8.9Hz),  
7.2-7.7 (4H, m), 7.78 (2H, d, J=8.9Hz), 7.94 (4H,  
s), 8.07 (1H, m), 8.54 (1H, m), 8.80 (1H, s), 8.95  
(1H, s)

15 MASS (m/z) : 1334.63 (M-Na<sup>+</sup>)

Example 152

IR (KBr) : 3353, 2927, 1675, 1650, 1538, 1513, 1456, 1396,  
1340, 1238, 1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.95 (3H, d, J=6.7Hz), 1.0-1.4 (8H,  
20 m), 1.58 (1H, m), 1.78 (4H, m), 1.8-2.1 (3H, m),  
2.1-2.6 (5H, m), 2.63 (4H, m), 2.98 (2H, m), 3.20  
(1H, m), 3.4 (4H, m), 3.74 (2H, m), 3.8-4.6 (12H,  
m), 4.6-5.6 (9H, m), 6.72 (1H, d, J=8.2Hz), 6.81 (1H,  
d, J=8.2Hz), 6.88 (1H, s), 7.04 (1H, s), 7.08 (2H,  
25 d, J=8.9Hz), 7.2-7.7 (4H, m), 7.77 (2H, d, J=8.9Hz),  
7.94 (4H, s), 8.10 (1H, m), 8.58 (1H, m), 8.80 (1H,  
s), 8.95 (1H, s)

MASS (m/z) : 1388.3 (M-Na<sup>+</sup>)

Example 153

30 IR (KBr) : 3353, 2931, 1668, 1650, 1631, 1537, 1513, 1456,  
1396, 1270, 1238, 1197 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.97 (3H, d, J=6.7Hz), 1.0-1.4 (8H,  
m), 1.58 (1H, m), 1.75 (4H, m), 1.7-2.1 (3H, m),  
2.1-2.6 (7H, m), 2.63 (4H, m), 2.98 (2H, m), 3.20  
35 (1H, m), 3.4 (4H, m), 3.74 (2H, m), 3.8-4.6 (11H,



m), 4.6-5.6 (8H, m), 6.72 (1H, d, J=8.2Hz), 6.81 (1H, d, J=8.2Hz), 6.88 (1H, s), 7.04 (1H, s), 7.08 (2H, d, J=8.9Hz), 7.2-7.7 (4H, m), 7.77 (2H, d, J=8.9Hz), 7.94 (4H, s), 8.11 (1H, m), 8.58 (1H, m), 8.80 (1H, s), 8.95 (1H, s)

MASS (m/z) : 1372.3 (M-Na<sup>+</sup>)

Example 154

IR (KBr) : 3353, 2935, 1666, 1633, 1540, 1513, 1461, 1440, 1247 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.9-1.1 (6H, m), 1.10 (3H, d, J=5.7Hz), 1.47 (2H, m), 1.6-2.1 (5H, m), 2.1-2.6 (4H, m), 2.98 (2H, m), 3.20 (1H, m), 3.71 (2H, m), 3.8-4.6 (14H, m), 4.6-5.6 (9H, m), 6.67 (1H, d, J=8.2Hz), 6.79 (1H, d, J=8.2Hz), 6.88 (1H, s), 6.99 (2H, d, J=8.8Hz), 7.05 (1H, s), 7.2-7.7 (4H, m), 7.82 (2H, d, J=8.8Hz), 7.97 (4H, s), 8.10 (1H, m), 8.58 (1H, m), 8.66 (1H, s), 8.78 (1H, s)

MASS (m/z) : 1294.53 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>56</sub>H<sub>68</sub>N<sub>11</sub>NaO<sub>21</sub>S<sub>2</sub>·9H<sub>2</sub>O :

C 45.43, H 5.85, N 10.41  
Found : C 45.52, H 5.81, N 10.41

Example 155

IR (KBr) : 3361, 2935, 1650, 1631, 1540, 1515, 1463, 1442, 1247, 1047 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>, δ) : 0.9-1.1 (6H, m), 1.10 (3H, d, J=5.7Hz), 1.2-1.5 (4H, m), 1.6-2.1 (5H, m), 2.1-2.6 (4H, m), 2.98 (2H, m), 3.20 (1H, m), 3.71 (2H, m), 3.8-4.6 (14H, m), 4.6-5.6 (9H, m), 6.69 (2H, d, J=8.2Hz), 6.80 (1H, d, J=8.2Hz), 6.87 (1H, s), 6.99 (2H, d, J=8.8Hz), 7.05 (1H, s), 7.2-7.7 (4H, m), 7.82 (2H, d, J=8.8Hz), 8.06 (4H, s), 8.10 (1H, m), 8.58 (1H, m), 8.67 (1H, s), 8.76 (1H, s)

MASS (m/z) : 1308.25 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>57</sub>H<sub>70</sub>N<sub>11</sub>NaO<sub>21</sub>S<sub>2</sub>·8H<sub>2</sub>O :

C 46.37, H 5.87, N 10.44

Found : C 46.29, H 5.44, N 10.19

Example 156

IR (KBr) : 3359, 2933, 1666, 1631, 1540, 1513, 1463, 1440,  
1295, 1247, 1047  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.9-1.1 (6H, m), 1.10 (3H, d,  $J=5.7\text{Hz}$ ),  
1.2-1.5 (6H, m), 1.6-2.1 (5H, m), 2.1-2.6 (4H, m),  
2.98 (2H, m), 3.20 (1H, m), 3.71 (2H, m), 3.8-4.6  
(14H, m), 4.6-5.6 (9H, m), 6.69 (1H, d,  $J=8.2\text{Hz}$ ),  
6.79 (1H, d,  $J=8.2\text{Hz}$ ), 6.87 (1H, s), 6.98 (2H, d,  
10  $J=8.8\text{Hz}$ ), 7.04 (1H, s), 7.2-7.7 (4H, m), 7.82 (2H,  
d,  $J=8.8\text{Hz}$ ), 8.06 (4H, s), 8.10 (1H, m), 8.58 (1H,  
m), 8.67 (1H, s), 8.77 (1H, s)

MASS (m/z) : 1322.61 (M- $\text{Na}^+$ )

Elemental Analysis Calcd. For  $\text{C}_{58}\text{H}_{72}\text{N}_{11}\text{NaO}_{21}\text{S}_2 \cdot 11\text{H}_2\text{O}$  :

15 C 45.10, H 6.13, N 9.98

Found : C 45.31, H 5.81, N 9.84

Example 157

IR (KBr) : 3351, 2933, 1631, 1523, 1465, 1440, 1255,  
1178, 1047  $\text{cm}^{-1}$

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.8-1.0 (6H, m), 1.10 (3H, d,  $J=5.7\text{Hz}$ ),  
1.2-1.6 (6H, m), 1.6-2.1 (5H, m), 2.1-2.5 (4H, m),  
2.98 (2H, m), 3.20 (1H, m), 3.73 (2H, m), 3.8-4.6  
(14H, m), 4.6-5.4 (9H, m), 6.69 (1H, d,  $J=8.2\text{Hz}$ ),  
6.79 (1H, d,  $J=8.2\text{Hz}$ ), 6.88 (1H, s), 7.05 (1H, s),  
25 7.14 (2H, d,  $J=8.8\text{Hz}$ ), 7.23 (1H, m), 7.3-7.5 (2H,  
m), 7.67 (1H, m), 7.89 (2H, d,  $J=8.8\text{Hz}$ ), 7.96 (4H,  
s), 8.07 (1H, m), 8.54 (1H, m), 8.85 (1H, s), 8.95  
(1H, s)

MASS (m/z) : 1322.12 (M- $\text{Na}^+$ )

30 Elemental Analysis Calcd. For  $\text{C}_{58}\text{H}_{72}\text{N}_{11}\text{NaO}_{21}\text{S}_2 \cdot 8\text{H}_2\text{O}$  :

C 46.74, H 5.95, N 10.34

Found : C 46.81, H 5.67, N 10.23

Example 158

IR (KBr) : 3359, 2935, 1652, 1631, 1538, 1523, 1429, 1382,  
35 1299, 1253, 1047  $\text{cm}^{-1}$

NMR (DMSO-d<sub>6</sub>, δ) : 0.8-1.0 (6H, m), 1.10 (3H, d, J=5.7Hz),  
1.3-1.5 (4H, m), 1.6-2.1 (5H, m), 2.1-2.5 (4H, m),  
2.98 (2H, m), 3.20 (1H, m), 3.75 (2H, s), 3.8-4.6  
(14H, m), 4.6-5.4 (9H, m), 6.69 (1H, d, J=8.2Hz),  
5 6.77 (1H, d, J=8.2Hz), 6.85 (1H, s), 7.01 (2H, d,  
J=8.8Hz), 7.05 (1H, s), 7.23 (1H, m), 7.43 (2H, d,  
J=8.2Hz), 7.69 (1H, m), 7.77 (2H, d, J=8.8Hz), 7.87  
(2H, d, J=8.3Hz), 8.05 (1H, d, J=7.9Hz), 8.19 (2H, d,  
J=8.3Hz), 8.54 (1H, m), 8.61 (1H, d, J=6.7Hz), 8.82  
10 (1H, s)

MASS (m/z) : 1312.10 (M-Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>56</sub>H<sub>70</sub>N<sub>11</sub>NaO<sub>22</sub>S<sub>2</sub>·13H<sub>2</sub>O :

C 42.83, H 6.16, N 9.81

Found : C 42.83, H 5.39, N 9.75

15 Example 159

MASS (m/z) : 1429.04 (M-Na<sup>+</sup>)

Example 160

To a solution of 1-hydroxybenzotriazole (26 mg) and  
4-[5-[4-(4-propoxypiperidin-1-yl)phenyl]-1,3,4-thiadiazol-  
20 2-yl]benzoic acid hydrochloride (60 mg) in N,N-  
dimethylformamide (2.4 ml) was added 1-ethyl-3-(3'-  
dimethylaminopropyl)carbodiimide (48 μl) and the mixture was  
stirred for 19 hours at ambient temperature. Then to the  
reaction mixture was added Starting Compound (160) (120 mg)  
25 and N,N'-diisopropylethylamine (34 μl) and the mixture was  
stirred for 24 hours at ambient temperature. The reaction  
mixture was pulverized with ethyl acetate. The resulting  
precipitate was collected by filtration, washed with  
diisopropyl ether and dried under reduced pressure. The solid  
30 was added to saturated aqueous sodium hydrogen carbonate  
solution, subjected to column chromatography on ODS (YMC-gel  
ODS-AM S-50) and eluted with 20% acetonitrile in water. The  
fractions containing the object compound were combined and  
evaporated under reduced pressure to remove acetonitrile. The  
35 residue was lyophilized to give Object Compound (160) (48 mg)

as a yellow powder.

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.88 (3H, d, J=7.4Hz), 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d, J=5.6Hz), 1.38-2.47 (16H, m), 2.80-5.50 (30H, m), 6.70 (1H, d, J=8.2Hz), 6.81 (1H, d, J=8.2Hz), 6.87 (1H, s), 7.04 (1H, s), 7.09 (2H, d, J=9.2Hz), 7.26-7.76 (3H, m), 7.84 (2H, d, J=8.8Hz), 7.97-8.14 (6H, m), 8.64-8.95 (2H, m)

MASS (m/z) : 1347.44 (M-Na<sup>+</sup>)

The following compounds [Examples 161 and 162] were obtained in a manner similar to that of Example 160.

Example 161

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.96 (3H, d, J=6.6Hz), 1.10 (3H, d, J=5.6Hz), 1.68-2.50 (7H, m), 2.80-5.50 (34H, m), 6.71 (1H, d, J=8.2Hz), 6.80 (1H, d, J=8.2Hz), 6.86 (1H, s), 6.76-6.94 (1H, m), 6.94-7.09 (3H, m), 7.09-7.34 (4H, m), 7.34-7.78 (3H, m), 7.90 (2H, d, J=8.7Hz), 7.96-8.17 (6H, m), 8.49-8.88 (2H, m)

MASS (m/z) : 1343.23 (M-Na<sup>+</sup>)

Example 162

IR (KBr) : 1655, 1527 cm<sup>-1</sup>

NMR (DMSO-d<sub>6</sub>,  $\delta$ ) : 0.97 (3H, d, J=6.8Hz), 1.10 (3H, d, J=5.7Hz), 1.8-2.6 (12H, m), 2.8-3.6 (7H, m), 3.7-4.6 (14H, m), 4.7-5.5 (8H, m), 6.6-6.85 (4H, m), 6.85-6.95 (1H, m), 6.97 (1H, s), 7.15-7.25 (1H, m), 7.4-7.8 (3H, m), 7.72 (2H, d, J=8.9Hz), 8.0-8.2 (5H, m), 8.30 (1H, s), 8.71 (1H, s), 8.7-8.9 (1H, m), 9.11 (1H, s)

MASS (m/z) : 1302 (M<sup>+</sup>-23)

Elemental Analysis Calcd. For C<sub>57</sub>H<sub>68</sub>N<sub>13</sub>NaO<sub>19</sub>S<sub>2</sub>·9H<sub>2</sub>O :

Found : C 45.99, H 5.82, N 12.23  
C 45.92, H 5.73, N 12.09

Example 163

To a solution of Starting Compound (163) (2.0 g) in trifluoroacetic acid (48 ml) was added 1N hydrochloric acid (8 ml) with stirring at ambient temperature. The mixture was

stirred at the same temperature overnight. The reaction mixture was evaporated to remove trifluoroacetic acid under reduced pressure. To the residue were added standard solution (pH 6.86) (100 ml) and acetonitrile (50 ml), and the solution was adjusted to pH 3 with 1N sodium hydroxide. The solution was chromatographed on reverse phase silica gel, YMC-gel ODS-AM 120-S50 (Trademark, made by YMC) (600 ml) eluting in turn with 20% aqueous acetonitrile (2 L), 30% aqueous acetonitrile (3 L), and 40% aqueous acetonitrile (4 L). The fractions containing the desired compound were collected and evaporated in vacuo to remove organic solvent. The resulting residue was lyophilized to give a white powder. The white powder was washed with ethyl acetate (30 ml) and dried in vacuo at ambient temperature for 3 hours to give Object Compound (163) (1.02 g).

NMR (DMSO- $d_6$ +D<sub>2</sub>O,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.09 (3H, d, J=6.0Hz), 1.25-1.60 (8H, m), 1.60-2.45 (10H, m), 2.80-3.10 (1H, m), 3.21 (3H, s), 3.30 (2H, t, J=6.4Hz), 3.60-4.50 (15H, m), 4.65-4.95 (2H, m), 6.41 (1H, d, J=8.3Hz), 6.50-6.70 (2H, m), 7.11 (1H, s), 7.16 (1H, s), 7.25-7.60 (2H, m), 7.85-8.25 (8H, m)

ESI-MASS (m/z) : 1255.08 (M<sup>+</sup>+Na<sup>+</sup>)

Elemental Analysis Calcd. For C<sub>58</sub>H<sub>76</sub>N<sub>10</sub>O<sub>18</sub>S·4H<sub>2</sub>O :

C 53.37, H 6.49, N 10.73  
Found : C 53.61, H 6.44, N 10.84

#### Example 164

To a solution of the Starting Compound (164) (6.0 g) in a mixture of tetrahydrofuran (120 ml) and N,N-dimethylamide (30 ml) were added trimethylsilyl chloride (22.8 ml) and triethylamine (37.6 ml) with stirring under ice-cooling and the mixture was stood at ambient temperature overnight. To the reaction mixture was added tetrahydrofuran (50 ml). The resulting precipitates were filtered off. The filtrate was stood at 2-5°C overnight and evaporated in vacuo. The residue

was dissolved in a mixture of hexane (50 ml) and ethyl acetate (50 ml) (1:1, v/v) and the solution was evaporated in vacuo to give a residue. The residue was chromatographed on silica gel (600 ml) eluting in turn with a mixture of hexane and ethyl acetate (3:2, v/v) and a mixture of hexane and ethyl acetate (1:1, v/v). The fractions containing the desired compound were collected and evaporated in vacuo. The resulting residue (5.68 g) was dissolved in a mixture of acetonitrile (30 ml) and methanol (30 ml). To the solution were added in turn diisopropylethylamine (1.68 ml) and trimethylsilyldiazomethane (4.82 ml) with stirring at ambient temperature and the mixture was allowed to stand at the same temperature overnight. To the reaction mixture were added ethyl acetate (150 ml) and saturated aqueous hydrogen carbonate solution (100 ml). The organic layer was separated, washed with saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate and evaporated in vacuo to give a residue. The residue was dissolved in a mixture of tetrahydrofuran (30 ml) and acetic acid (3.68 ml). To the solution was added 1M solution of tetrabutyl ammonium fluoride in water with stirring under ice-cooling and the mixture was stirred at the same temperature for 4 hours. The reaction mixture was evaporated in vacuo and dissolved in 20% aqueous acetonitrile. The solution was chromatographed on reverse phase silica gel, YMC-gel ODS-AM 120-S50 (Trademark, made by YMC) (700 ml) eluting in turn with 20% aqueous acetonitrile (3.5 L), 30% aqueous acetonitrile (3.5 L) and 40% aqueous acetonitrile (3.5 L). The fractions containing the desired compound were collected and evaporated in vacuo to remove organic solvent. The resulting residue was lyophilized to give a white powder. The white powder was purified by liquid chromatography eluting with 38% acetonitrile in pH 6.86 standard buffer solution to give two compounds.

The first compound was chromatographed on reverse phase silica gel, YMC-gel ODS-AM 120-S50 (Trademark, made by YMC)

(700 ml) eluting in turn with 20% aqueous acetonitrile (3.5 L) and 50% aqueous acetonitrile (3.5 L). The fractions containing the desired compound were collected and evaporated in vacuo to remove organic solvent. The resulting residue was lyophilized to give Object Compound (164-I) (1.37 g).

The other Object Compound (164-II) was chromatographed on reverse phase silica gel, YMC-gel ODS-AM 120-S50 (Trademark, made by YMC) (700 ml) eluting in turn with 20% aqueous acetonitrile (3.5 L) and 50% aqueous acetonitrile (3.5 L). The fractions containing the desired compound were collected and evaporated in vacuo to remove organic solvent. The resulting residue was lyophilized to give Object Compound (164-II) (275 mg).

Object Compound (164-I)

NMR (DMSO- $d_6$ +D $_2$ O,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.09 (3H, d, J=6.1Hz), 1.25-2.50 (19H, m), 2.85-3.00 (1H, m), 3.74 (3H, s), 3.31 (2H, t, J=6.4Hz), 3.75-4.55 (17H, m), 4.70-5.00 (2H, m), 6.40-6.70 (3H, m), 7.14 (2H, d, J=8.9Hz), 7.98 (2H, d, J=8.9Hz), 8.05 (2H, d, J=8.7Hz), 8.12 (2H, d, J=8.7Hz)

ESI-MASS (m/z) : 1269.4 ( $M^+$ +Na $^+$ ) (positive)

1246.4 ( $M^+$ -1) (negative)

Elemental Analysis Calcd. For C $_{59}$ H $_{78}$ N $_{10}$ O $_{18}$ S $\cdot$ 3H $_2$ O :

C 54.45, H 6.51, N 10.76

Found : C 54.11, H 6.74, N 11.18

Object Compound (164-II)

NMR (DMSO- $d_6$ +D $_2$ O,  $\delta$ ) : 0.96 (3H, d, J=6.7Hz), 1.10 (3H, d, J=6.1Hz), 1.20-2.45 (19H, m), 3.72 (3H, s), 3.73 (3H, s), 3.80-5.00 (15H, m), 6.55-6.90 (3H, m), 7.13 (2H, d, J=8.9Hz), 7.97 (2H, d, J=8.9Hz), 8.00-8.20 (4H, m)

ESI-MASS (m/z) : 1283.4 ( $M$ +Na $^+$ ) (positive)

The following compound was obtained according to a similar manner by using tert-butyldimethylsilane instead of tert-butyldimethylsilane of Example 6.

Example 165

The following compound was obtained in a manner similar to that of Example 2-3 of WO97/32975.

Example 166

- 5 IR (KBr) : 3394, 3327, 1676, 1633, 1439  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.8\text{Hz}$ ), 1.08 (3H, d,  $J=6.0\text{Hz}$ ), 1.88-5.83 (35H, m), 6.68-8.71 (10H, m)  
MASS (m/z) : 903.17 (M- $\text{Na}^+$ )

Example 167

- 10 To a solution of Starting Compound (167) (0.1 g) and  
4-[5-[4-(7-methoxyheptyloxy)phenyl]-1,3,4-thiadiazol-2-  
yl]benzoic acid benzotriazol-1-yl ester (66.1 mg) in  
dimethylformamide (1 ml) was added diisopropylethylamine  
(0.029 ml) and the mixture was stirred for 5 hours at ambient  
15 temperature. The reaction mixture was pulverized with ethyl  
acetate. The precipitate was collected by filtration and  
dried under reduced pressure to give Object Compound (167) (159  
mg).

- IR (KBr) : 3344, 1648.8, 1637.3, 1513.8, 1257.4,  
20 1043.3  $\text{cm}^{-1}$   
NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.97 (3H, d,  $J=6.6\text{Hz}$ ), 1.10 (3H, d,  $J=5.6\text{Hz}$ ), 1.2-1.6 (23H, m), 1.6-2.6 (12H, m),  
2.9-4.6 (25H, m), 4.7-5.5 (9H, m), 6.71 (1H, d,  $J=8.2\text{Hz}$ ), 6.78 (1H, d,  $J=8.2\text{Hz}$ ), 6.88 (1H, s), 6.97  
25 (1H, s), 7.13 (2H, d,  $J=8.8\text{Hz}$ ), 7.16 (1H, s), 7.44  
(1H, d,  $J=8.0\text{Hz}$ ), 7.59 (1H, br s), 7.70 (1H, brs),  
7.97 (2H, d,  $J=8.8\text{Hz}$ ), 7.9-8.2 (6H, m), 8.72 (1H,  
s), 8.79 (1H, d,  $J=7.3\text{Hz}$ )

- MASS (m/z) : 1311 (M-diisopropylamine-1)  
30 Elemental Analysis Calcd. For  $\text{C}_{66}\text{H}_{95}\text{N}_{11}\text{O}_{21}\text{S}_2 \cdot 5\text{H}_2\text{O}$  :  
C 51.72, H 6.90, N 10.05  
Found : C 51.89, H 6.57, N 9.98

The following compound was obtained in a manner similar to that of Example 167.



Example 168

IR (KBr) : 3344, 1664.3, 1633.4, 1506.1, 1436.7,  
1257.4  $\text{cm}^{-1}$

5 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.91 (3H, t,  $J=7.0\text{Hz}$ ), 0.97 (3H, d,  
 $J=6.6\text{Hz}$ ), 1.10 (3H, d,  $J=5.6\text{Hz}$ ), 1.0-1.5 (19H, m),  
1.6-2.7 (10H, m), 3.0-3.3 (3H, m), 3.7-4.6 (15H, m),  
4.8-5.3 (11H, m), 5.54 (1H, d,  $J=5.6\text{Hz}$ ), 6.73 (1H,  
d,  $J=8.2\text{Hz}$ ), 6.83 (1H, dd,  $J=8.2$  and  $1.5\text{Hz}$ ), 6.85  
10 (1H, s), 7.04 (1H, d,  $J=1.5\text{Hz}$ ), 7.12 (2H, d,  $J=8.8\text{Hz}$ ),  
7.2-7.5 (3H, m), 7.23 (1H, s), 7.56 (1H, s), 7.58  
(1H, m), 7.85 (2H, d,  $J=8.8\text{Hz}$ ), 7.9-8.1 (5H, m), 8.26  
(1H, d,  $J=8.7\text{Hz}$ ), 8.85 (1H, s), 8.87 (1H, d,  $J=7.3\text{Hz}$ )

MASS (m/z) : 1268 (M-diisopropylamine-1)

15 The following compound was obtained in a manner similar  
to that of Example 2-3 of WO97/32975.

Example 169

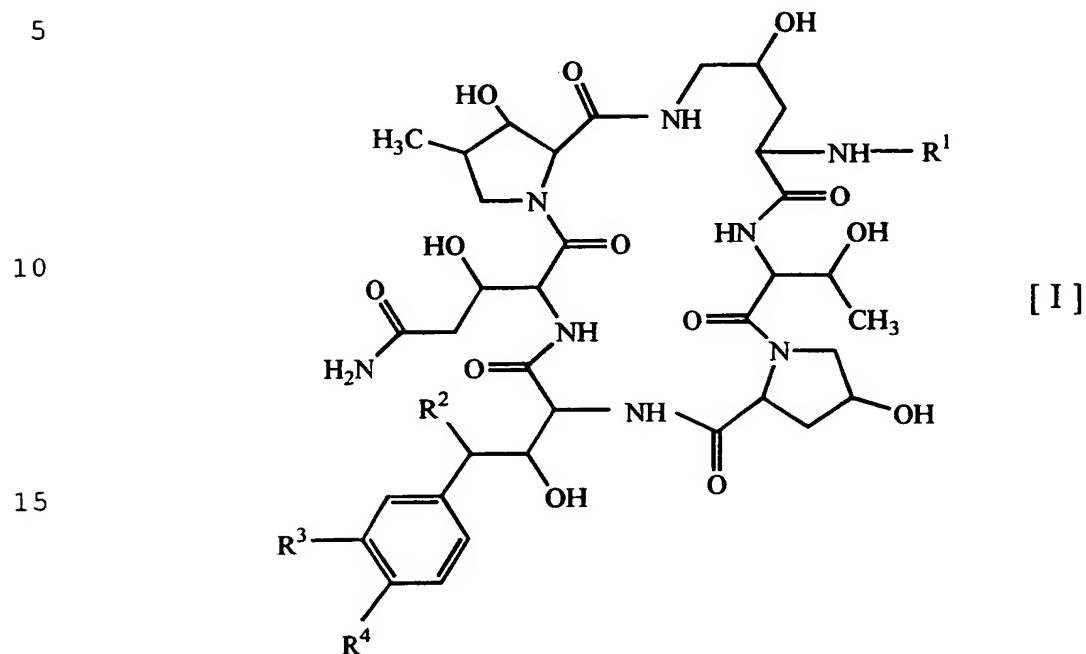
IR (KBr) : 1664, 1627, 1234, 1086, 1043  $\text{cm}^{-1}$

20 NMR (DMSO- $\text{d}_6$ ,  $\delta$ ) : 0.96 (3H, d,  $J=6.7\text{Hz}$ ), 1.14 (3H, d,  
 $J=5.9\text{Hz}$ ), 1.3-2.55 (8H, m), 2.6-3.6 (3H, m),  
3.65-4.5 (15H, m), 4.7-5.4 (7H, m), 6.65-7.05 (4H,  
m), 7.07 (1H, s), 7.4-8.25 (7H, m), 8.71 (1H, s)

MASS (m/z) : 903 (M-1)

## CLAIMS

1. A polypeptide compound of following the general formula [I]:



wherein

- 20  $R^1$  is hydrogen;  
 arylamino (lower) alkanoyl which may have one or  
 more suitable substituent(s);  
 aroyl substituted with heterocyclic group which  
 may have one or more suitable substituent(s);  
 25 aroyl substituted with aryl having higher  
 alkyl;  
 aroyl substituted with aryl having lower alkyl;  
 aryl( $C_2-C_6$ ) alkanoyl substituted with aryl  
 having lower alkyl;  
 30 lower alkanoyl substituted with unsaturated  
 condensed heterocyclic group which may have one or  
 more suitable substituent(s);  
 lower alkanoyl substituted with pyridyl which  
 may have one or more suitable substituent(s);  
 35 amino protective group;

heptylnaphthoyl;

hexylnaphthoyl;

aroyl substituted with heterocyclic carbamoyl  
which may have one or more suitable substituent(s);

5 lower alkanoyl substituted with  
cyclo(lower)alkyl which may have one or more suitable  
substituent(s);

lower alkanoyl substituted with thienyl having  
heterocyclic group which may have one or more  
10 suitable substituent(s); or

lower alkenoyl substituted with heterocyclic  
group which may have one or more suitable  
substituent(s),

$R^2$  is hydrogen or hydroxy,

15  $R^3$  is hydroxy, hydroxysulfonyloxy or lower alkoxy,  
and

$R^4$  is hydroxy or lower alkoxy,  
or a salt thereof.

20 2. A compound of claim 1, wherein

$R^1$  is aroyl substituted with heterocyclic group which  
may have one or more suitable substituent(s).

3. A compound of claim 2, wherein

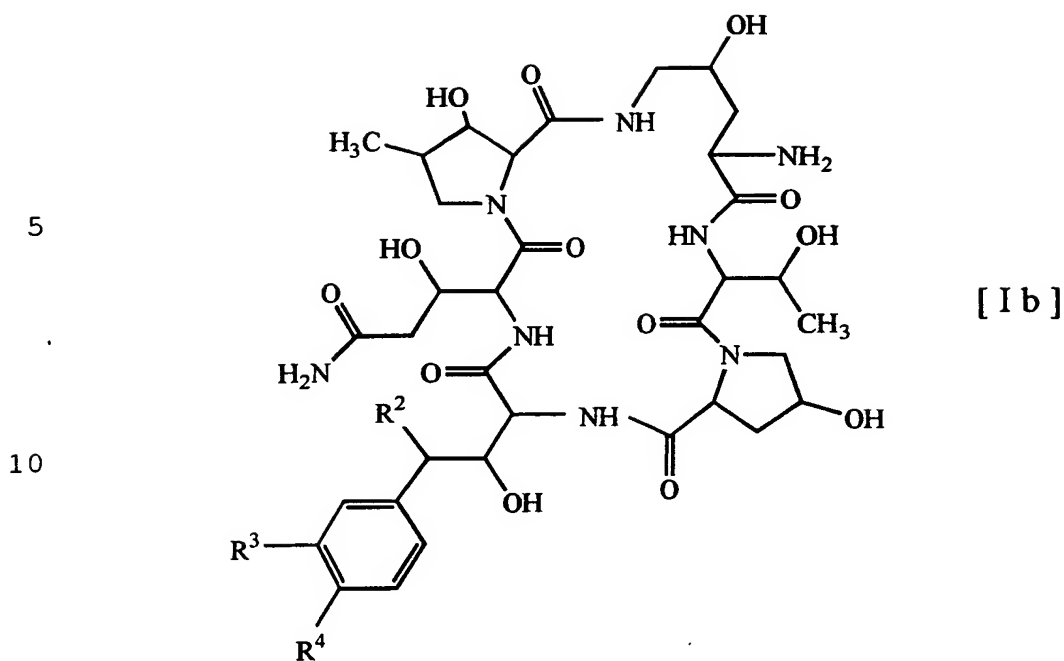
25  $R^1$  is benzoyl substituted with unsaturated 3 to 8-  
membered heteromonocyclic group containing 1 or 2  
sulfur atom(s) and 1 to 3 nitrogen atom(s) having  
phenyl which has a suitable substituent selected  
from the group consisting of saturated 3 to 8-  
30 membered heteromonocyclic group containing 1 to 4  
nitrogen atom(s) which may have cyclo(lower)alkyl  
having di(lower)alkyl, lower alkoxy(lower)alkoxy,  
lower alkoxy(higher)alkoxy and phenyl substituted  
with saturated 3 to 8-membered heteromonocyclic  
35 group containing 1 or 2 oxygen atom(s) and 1 to 3

nitrogen atom(s) having di(lower)alkyl; or  
benzoyl substituted with unsaturated  
condensed heterocyclic group containing 1 or 2  
sulfur atom(s) and 1 to 3 nitrogen atom(s) having  
phenyl which has lower alkoxy.

4. A compound of claim 3, wherein  
R<sup>1</sup> is benzoyl substituted with thiadiazolyl which  
has phenyl having piperidyl,  
benzoyl substituted with thiadiazolyl which  
has phenyl having lower alkoxy(lower)alkoxy,  
benzoyl substituted with thiadiazolyl which  
has phenyl having lower alkoxy(higher)alkoxy,  
benzoyl substituted with thiadiazolyl having  
phenyl which has piperazinyl substituted with  
cyclohexyl,  
benzoyl substituted with thiadiazolyl having  
phenyl substituted with phenyl which has morpholino  
having di(lower)alkyl, or  
benzoyl substituted with imidazothiadiazolyl  
having phenyl which has lower alkoxy.

5. A compound of claim 4, wherein  
R<sup>1</sup> is benzoyl substituted with thiadiazolyl which  
has phenyl having piperidyl, or  
benzoyl substituted with thiadiazolyl which  
has phenyl having lower alkoxy(higher)alkoxy,  
R<sup>3</sup> is hydroxysulfonyloxy, and  
R<sup>4</sup> is hydroxy.

6. A process for preparing a polypeptide compound [I]  
of claim 1 or a salt thereof,  
which comprises,  
i) reacting a compound [Ib] of the formula :



wherein

$R^2$ ,  $R^3$  and  $R^4$  are as defined in Claim 1 or its reactive derivative at the amino group or a salt thereof, with a compound [III] of the formula :



wherein

$R_a^1$  is arylamino(lower)alkanoyl which may have one or more suitable substituent(s);

aryl substituted with heterocyclic group which may have one or more suitable substituent(s);

25 aryl substituted with aryl having higher alkyl;

aryl substituted with aryl having lower alkyl;

aryl( $C_2$ - $C_6$ )alkanoyl substituted with aryl having lower alkyl;

30 lower alkanoyl substituted with unsaturated condensed heterocyclic group which may have one or more suitable substituent(s);

lower alkanoyl substituted with pyridyl which  
may have one or more suitable substituent(s);

amino protective group;

heptylnaphthoyl;

5 hexylnaphthoyl;

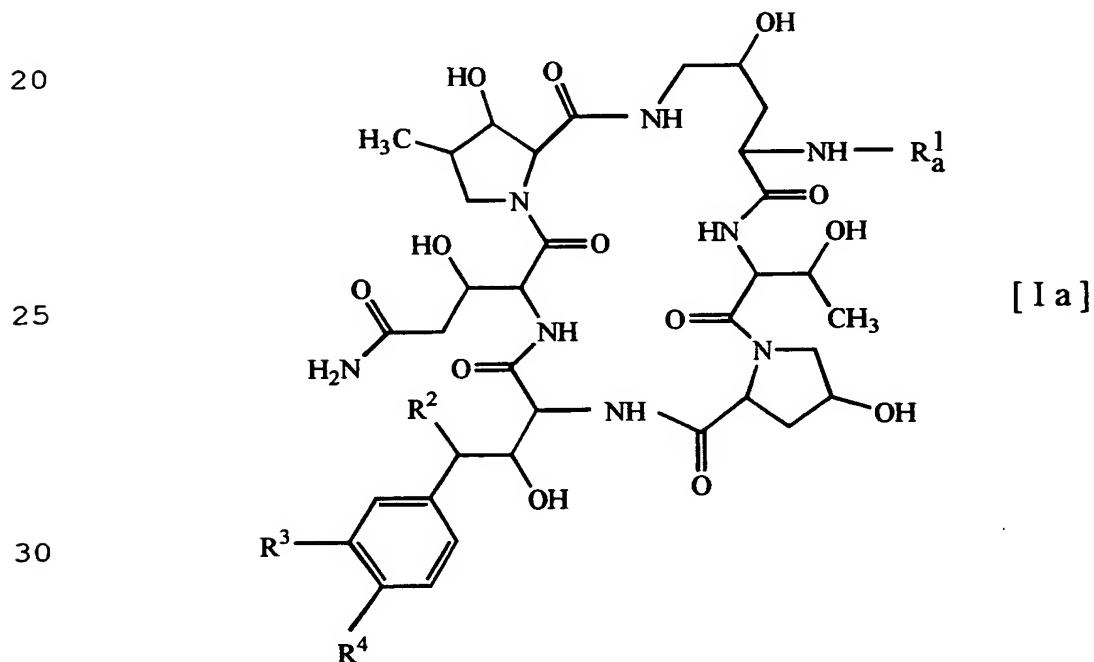
aroyl substituted with heterocyclic carbamoyl  
which may have one or more suitable substituent(s);

lower alkanoyl substituted with  
cyclo(lower)alkyl which may have one or more suitable  
10 substituent(s);

lower alkanoyl substituted with thienyl having  
heterocyclic group which may have one or more  
suitable substituent(s); or

lower alkenoyl substituted with heterocyclic  
15 group which may have one or more suitable  
substituent(s),

or its reactive derivative at the carboxy group or a salt  
thereof, to give a compound [Ia] of the formula:



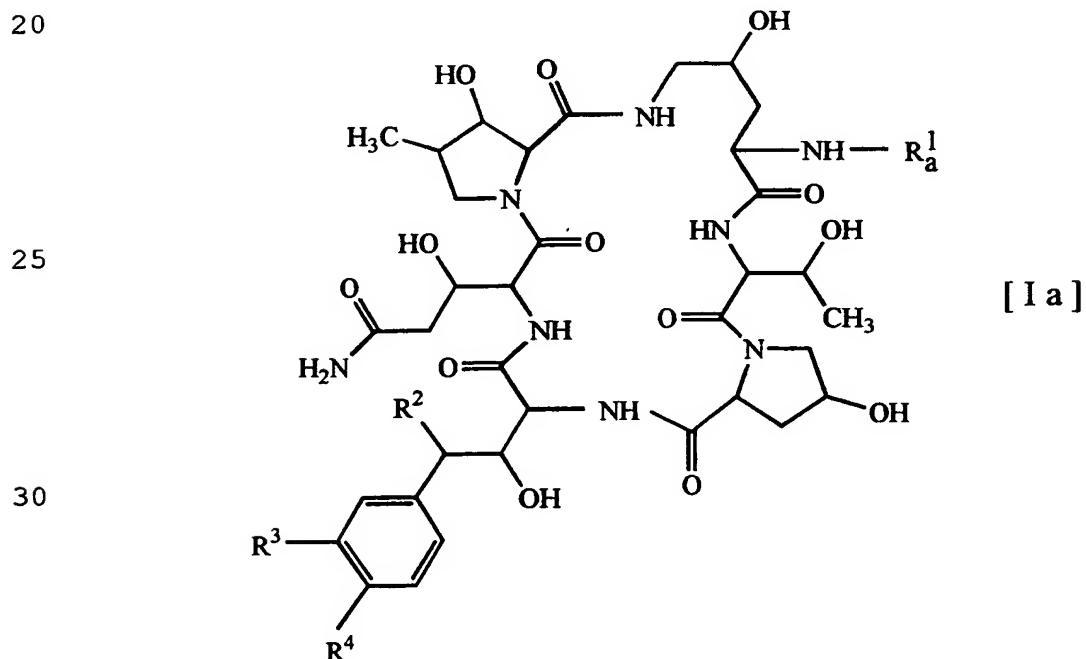
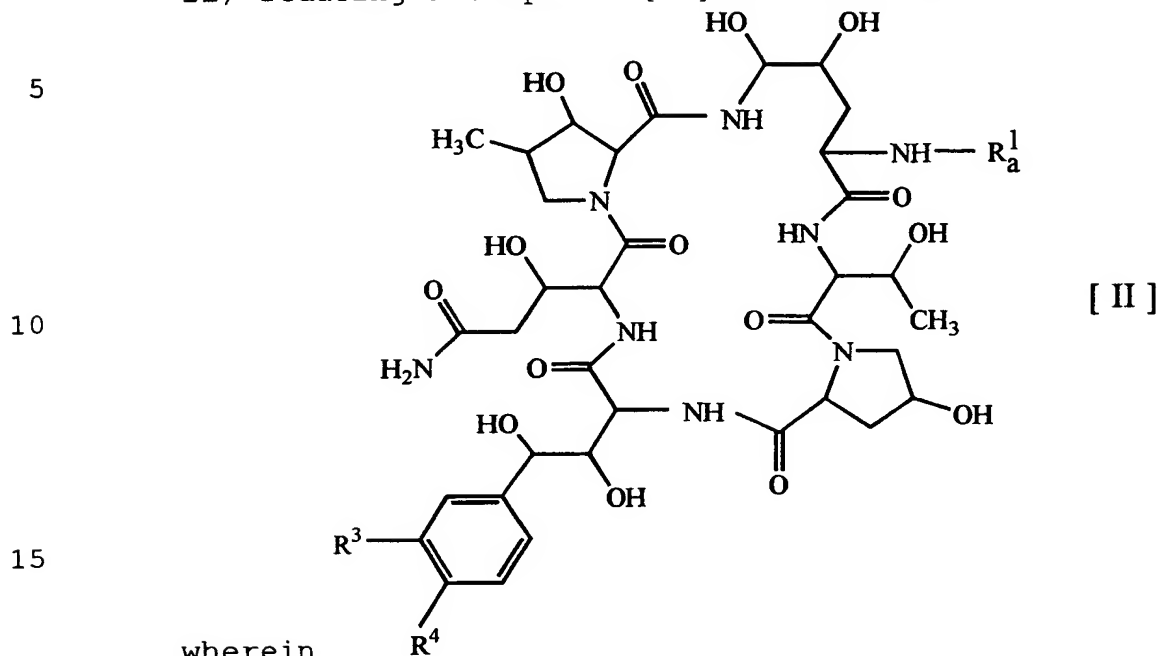
wherein

$R^2$ ,  $R^3$  and  $R^4$  are as defined in Claim 1, and

$R_a^1$  is as defined above

or a salt thereof, or

ii) reducing a compound [II] of the formula:



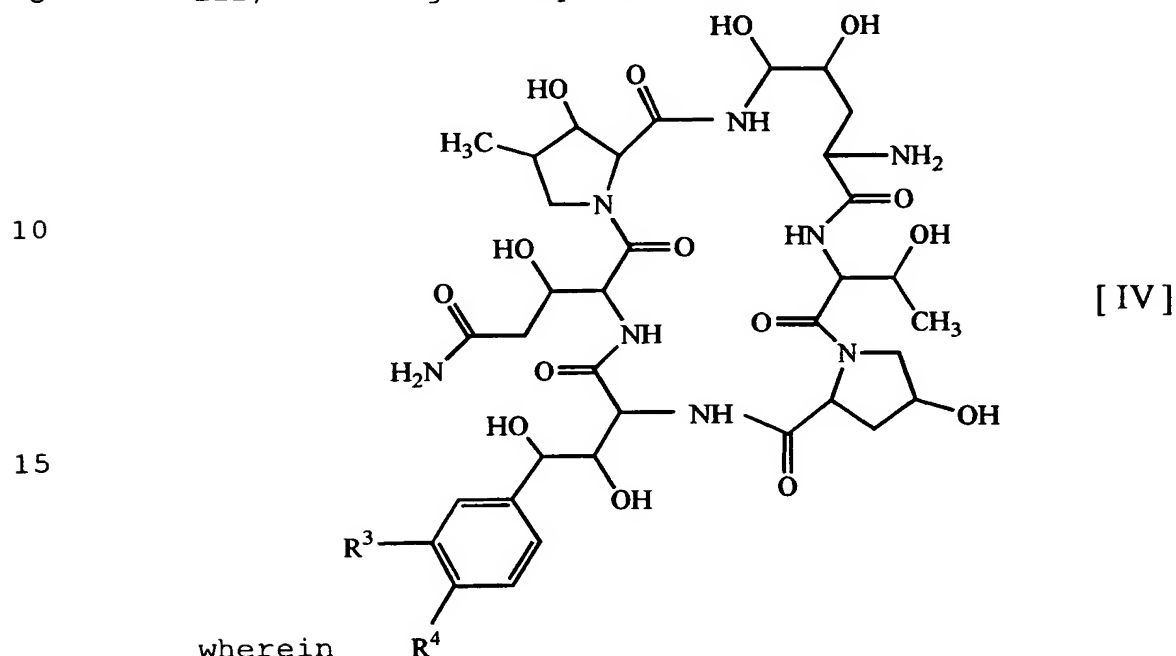
wherein

$R^2$ ,  $R^3$  and  $R^4$  are as defined in Claim 1, and

$R_a^1$  is as defined above,

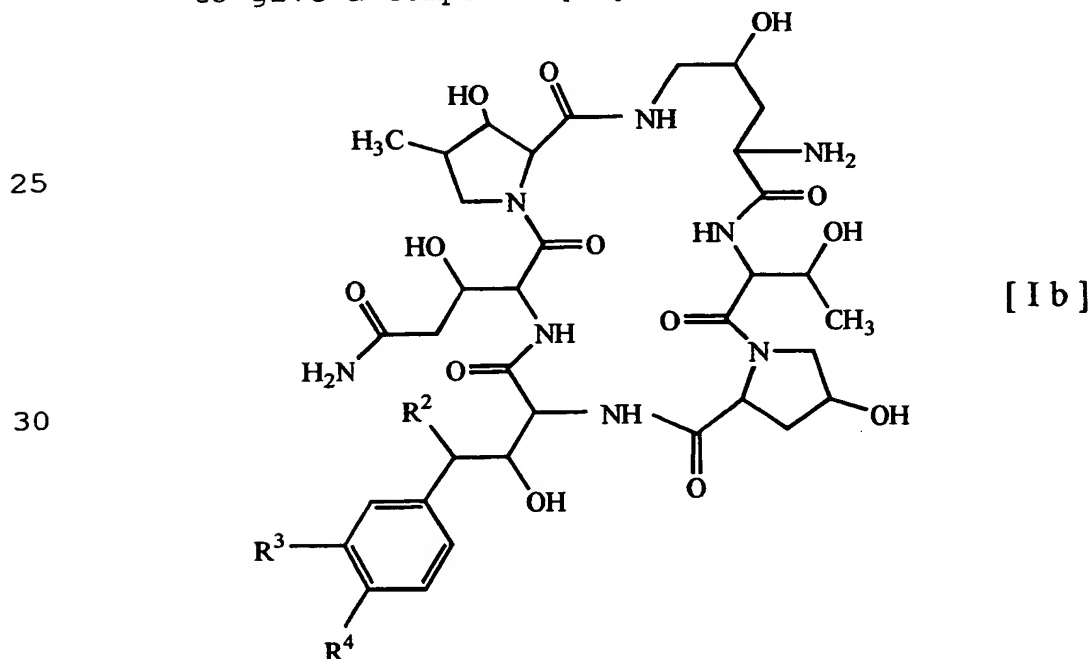
or a salt thereof, or

5     iii) reducing a compound [IV] of the formula :



wherein

20      $R^3$  and  $R^4$  are as defined in Claim 1, or a salt thereof,  
to give a compound [Ib] of the formula:





wherein

$R^2$ ,  $R^3$  and  $R^4$  are as defined in Claim 1,  
or a salt thereof.

- 5    7.    A pharmaceutical composition which comprises, as an  
active ingredient, a compound of Claim 1 or a  
pharmaceutically acceptable salt thereof in admixture  
with pharmaceutically acceptable carrier or excipients.
- 10   8.    Use of a compound of Claim 1 or a pharmaceutically  
acceptable salt thereof as a medicament.
9.    A compound of Claim 1 or a pharmaceutically acceptable  
salt thereof for use as a medicament.
- 15
10.   A method for the prophylactic and/or therapeutic  
treatment of infectious diseases caused by pathogenic  
microorganisms, which comprises administering a compound  
of claim 1 or a pharmaceutically acceptable salt thereof  
20   to a human being or an animal.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 99/00538

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 C07K7/56 A61K38/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 644 199 A (FUJISAWA PHARMACEUTICAL CO) 22 March 1995	1,6-10
Y	see the whole document	2-5
Y	WO 96 11210 A (FUJISAWA PHARMACEUTICAL CO ;OHKI HIDENORI (JP); TOMISHIMA MASAKI ()) 18 April 1996 cited in the application The whole document; see esp. examples 90 and 116	2-5



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

11 May 1999

Date of mailing of the international search report

21/05/1999

Name and mailing address of the ISA  
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Authorized officer

Groenendijk, M

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP 99/00538

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 8, 10  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim(s) 8, 10  
is(are) directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 99/00538

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